Boston Drug Laboratory GC/MS Protocol

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1. Introduction

This document is a Standard Operating Procedure (SOP) for the Drug Analysis Gas Chromatography-Mass Spectrometry (GC-MS) Laboratory. The principles introduced in this SOP will apply to all forensic items confirmed via GC/MS, both routine and specialty drug submissions.

GC-MS is the primary instrument used to structurally identify controlled substances submitted to the laboratory. GC/MS is a separation and identification technique used to analyze volatile compounds. Components of a mixture are volatilized in a heated injector and subsequently separated in a capillary column coated with a thin film of liquid. A vaporized sample will dissolve in the stationary liquid phase and then re-vaporize in the mobile gas stream as it travels through the column. Dissimilar distribution coefficients in the two phases are the driving force for GC separation. Retention is mainly influenced by a compounds boiling point or vapor pressure, oven temperature, carrier gas flow rate, polarity of the column, column film thickness, column diameter and length. Components elute into an electron impact-mass selective detector (EI-MSD). The mass spectrometer performs three basic functions: ionization in the source body, mass separation in the quadrupole and ion detection by an electron multiplier. All three functions are performed under vacuum conditions as components elute from the column. Low operating pressures are necessary for an adequate mean free path-an ion's average distance traveled between collisions. Ions must be able to travel from their point of origin to the detector without colliding with air, non-ionized molecules or the instrument. Collisions mean an ion may not be detected at all (scattered or neutralized) or incorrectly identified because of intermolecular reactions.

Ionization- A heated filament on the ion source body bombards eluting compounds with electrons. Ion source filaments emit electrons of a certain **energy** level (70 eV for "classical" spectra) using a specific **emission current** that determines the number of electrons used for ionization. Ionization removes one valence shell electron from the analyte molecule, creating a positively charged ionic species known as the parent compound or molecular ion (M+.). As the electron passes close to the molecule, the negative charge of the electron repels and distorts the electron cloud surrounding the molecule. This distortion transfers kinetic energy from the moving electron to the electron cloud of the molecule. If enough energy is transferred, a valence electron will be ejected to form a cation radical. These ions exist in an excited energy state and fragment into other cations, neutral species and radicals, species with no charge but with an unpaired electron. Charged species are then pushed out of the source into the **quadrupole** by the **repeller** and voltages applied to the **ion focus lens/entrance lens.** See attachment 1A.

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Mass Separation- Separation occurs in a quadrupole mass filter consisting of four poles, or rods. In cross-section of a quadrupole, the four poles are arranged at the corners of a square. Diametrically charged rods work in tandem as a set. One set has a positive DC voltage applied to it. The other set has a negative DC voltage of the same value. In addition, all four rods have a superimposed RF voltage of alternating polarity, with the RF voltage 180 degrees out of phase for each rod. The m/z value transmitted through the quadrupole is determined by the electric field produced by the DC and RF voltages. Only if the ion has a particular m/z will its oscillation be stable in the mass filter and only this m/z will exit the end of the mass filter to be detected by the electron multiplier. The mass spectrum is scanned by varying the amplitude of the DC potential (U) and radio frequency potential (V), while keeping the RF frequency and U/V ratio constant. The intercept and slope are set empirically by simultaneously optimizing light and heavy masses to unit mass resolution. The concepts of **amu gain and offset** are represented in A**ttachment 1B**, otherwise known as the **Mathieu Stability Diagram.** It is a plot of DC voltage versus RF voltage and defines an ions stable trajectory in the quadrupole. The slope (U/V) mathematically represents amu gain and amu offset is the DC intercept on the y-axis. Increasing/decreasing the amu offset will have an equal effect on sensitivity across the entire mass range. Increasing/decreasing the amu gain will have an effect on low mass but a much greater effect on high mass. The determined values for amu gain/offset effect abundance and resolution by determining the cut-off for approximately constant peak widths. See **Attachment 2** by Randell Pedder for a discussion on Practical Quadrupole Theory.

Detection- In the 5973/5975, positively charged ions exiting the quadrupole are focused through a detector-focusing lens (**See Attachment 3**). Ions are subsequently deflected into the electron multiplier, located off-axis to the analyzer, by a **High Energy Dynode (HED).** The HED functions to accelerate ions into the multiplier and reduce the number of stray particles entering the detector. The HED (at –10,000 volts) attracts positively charged ions exiting the quadrupole, generating electrons that are attracted to the more positive electron multiplier (-3000 volts). The electrons hitting the surface of the electron multiplier liberate more electrons with every impact as they cascade down the horn. Every ionic particle that leaves the mass analyzer and enters the ion detector contains a given amount of electricity (10-19 coulomb per singly charged particle). As the number of ions arriving at the detector per unit time increases the amplified output of the detector increases proportionally. The electron multiplier amplifies the signal on the order of 10E5. At the end of the horn, the current generated by the electrons is carried out to a signal conditioning circuit.

The GC-MS chromatogram displays the total ion current (TIC) over time. Each peak in the TIC is the summation of all the ions specific to that molecule's fragmentation pattern. An identical fragmentation pattern can be reproduced from one instrument to another using similar experimental condition.

2. Objective

The objective of this SOP is to ensure operators handle submissions in a routine and predictable manner. The analytical data from the Drug Analysis GC/MS Laboratory is often used in criminal prosecutions and as a result, all samples will be analyzed in a manner consistent with forensic standards. Many elements of this protocol are designed to eliminate any appearance of doubt or uncertainty in the quality of laboratory's analytical findings.

3. Scope

All GC/MS operators will need to comply with the procedures set forth in this SOP. The GC/MS Laboratory will use standard forms and consistent guidelines to confirm all submissions. The following topics will be covered in this SOP: sample submission requirements and procedures, equipment maintenance and calibration, batch setup procedures, instrument and method QC, acceptance criteria for data analysis, reporting results, data backup, data retrieval and retention.

4. Responsibilities

-Chemist I, II, III and Supervisors are responsible for performing this SOP.
-The Chief of Laboratory will ensure compliance with this SOP.
-Senior Chemists/Laboratory Supervisor will monitor compliance with this SOP.
-The GC/MS Supervisor will oversee training of staff.

5. Related Documents

Training Guidelines for New Chemists
Commonwealth of Massachusetts
Department of Public Health
Drug Analysis Laboratory
Jamaica Plain, Ma 02130

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6. Definitions

Abundance- Describes the number of charged ions in the mass spectrometer.

Mass spectrometer: Instruments that bring a focused beam of ions to a fixed collector, where the ion current is detected electrically. These instruments measure the abundance of ions based on their m/z values.

TIC: Total Ion Current, synonymous with total ion abundance.

Molecular Ion: The removal of one valence shell electron from a compound to form a radical cation, also known as the parent ion.

Base Peak: The most intense peak in a displayed mass spectrum. Other peaks are normalized relative to the base peak.

Isomer: Different compounds that have the same molecular formula.

Standard Spectra Tune: Tuning optimizes the performance of the MSD by maximizing sensitivity while maintaining acceptable resolution and accurate mass assignment. Standard spectra tune is a tuning algorithm that ensures a standard response over the full mass range. The tuning compound PFTBA (Perfluorotributylamine) produces a characteristic spectrum that has mass 69 as the base peak and sets the relative abundances of mass 219 between 30 and 99 % and mass 502 greater than 1%. Standard Spectra Tune optimizes ion source components only to maximize the abundance of **mass 502**. Agilent's Standard Spectra Autotune (5971) is also referred to as a Standard Spectra Target Tune on the 5973/5975 since the relative target abundances of mass 50,131,219,414, and 502 are set at 1, 55, 45, 3.5 and 2.5. That is, the 5973/5975 MSD performs a target tune using standard spectra targets. Historically these targets have been used to duplicate spectral results from magnetic-sector instruments when most commercial libraries were created.

Carryover- A retained analyte in a GC's injection/ALS system that is detected in a blank. Carryover may originate from the syringe, the injector's liner, the injector's gas lines, the gold seal, the head of the column, or a contaminated blank. Carryover will have the same retention time for that analyte if it were normally injected. The TIC will have the ions for that analyte with varying degrees of intensity due to concentration. QC blanks may have other peaks due to late eluters, analytes that originated in the previous injection but did not elute before the end of the method's run time. Ghost peaks are a form of unpredictable carryover that is rarely seen. They typically have uncharacteristic retention times for an analyte and they may not resemble any analyte at all. Ghost peaks typically originate in a contaminated carrier line and their retention times can not be predicted. As a general rule, no method injects more than 1 uL of solvent.

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7. Equipment, Supplies and Reagents

Instruments

SYSTEM	GC MODEL/SERIAL#	MSD MODEL/SERIAL#
3	5890A/3310A48324	5971A/3306A04519
4	6890(G1530A)/US00025670	5973(G1098A)/US82311442
5	6890(G1530A)/US00026238	5973(1098A)/US82311436
6	6890N(G1530N)/CN10244001	5973NETWORK(G2577A)/US21843303
7	6890N(G1530N)/CN10724010	5975INERT/US65125812

SYSTEM	TOWER/SERIAL#	TRAY/SERIAL#
3	18593B/3534A43820	18596B/3506A33978
4	G2613A/US90204388	G2614A/US85203036
5	G2613A/US90204391	G2614A/US90203072
6	G2613A/CN30429193	G2614A/CN30423007
7	G2913A/CN72441374	G2614A/CN72244216

SYSTEM	PRINTER MODEL/SERIAL #
3	HP LASERJET 4/JPBH024544
4	HP LASERJET 4000/USMC071174
5	HP LASERJET 4000/USMC023436
6	HP LASERJET 4000/USMC071005
7	HP LASERJET 2420D/CNGJD23741 HP LASERJET P3005D/CND1D25603 STARTING 7/27/07

SYSTEM	COMPUTER MODEL/SERIAL NUMBER
4	Kayak XA 6/US83853841
5	Kayak XA 6/US83853197
6	HP Vectra VL420dt/us22109330
7	HP Compaq DC 7600/MXL6240TYF 1st computer 9/08/2006 /2UA6500K75 2nd computer 5/01/2006 HP Compaq DC7700/2ua723ok02 3rd computer 7/27/2007

Related Equipment

Agilent/HP Helium Multi-Stage Regulator 5183-4644
Supelco High Capacity Carrier Gas Purifier (oxygen and water) 2-3800-U
Powerware Prestige 3000 UPS
RadioShack OHM Meter
Commercial and Agilent Toolbox
Dell OptiPlex GX1 Computer networked to Instrumentation
Inlet Septum Remover
Gasmet Gas Flow Meter for 5971
Sanyo Air Conditioning Unit-Room temperature maintained at 70 degrees Fahrenheit

Consumable Supplies

Supelco OMI-2 Indicating Purifier and tube holder, 23906 and 23921
80 minute/700 MB CD-R/RW or 120 minute/4.7 GB DVD-R/RW with jewel case
Helium-Ultra High Purity
Supelco Split/Spitless Glass Liners, 4mm ID with deactivated glass wool, 2-048625
Therm-O-Ring ¼" Seals, liner o-ring, 21004-4-U
Supelco Gold plated Inlet Seals with nickel washer for Agilent, 23319-U
EI-MSD High Temperature Filaments Assembly, G2590-60053
Supelco Thermogreen LB-2 Septa, 10mm, 23156
Supelco Injector Column Nut, 24833-4
Supelco MSD Column Nut, 28034-U
Agilent Ferrule, 0.5 mm ID Graphite (short), 5080-8853
Agilent GC/MS Ferrule, 0.4mm ID hole, graphite/vespel, 5062-3508
HP-5MS Capillary Column, 0.25um (film) X 0.25mm (ID) X 30m (length)
Agilent 10 uL syringe (straight and tapered needle), 9301-0725 and 5181-3360

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Inland 45 Vacuum pump fluid or Pfeiffer P3 mineral oil
Micogrit, Type WCA, size 15
Fisherbrand Cotton Tipped Applicators, 6"
Kimble 11 mm vial caps, PFTE/Rubber
11 mm vial crimper
Kimble glass vials
Residue vials
9" Pasteur Capillary Pipets
Office Duster
Electron Multiplier Replacement Horn, 05971-80103
See Attachment 4 for a complete list of Standards

Reagents

Methanol- J.T. Baker, 9070-05, A.C.S. Reagent Grade, 4L
Chloroform- J.T. Baker, 9180-05, A.C.S. Reagent Grade, 4L
Acetone- Fisher, A9284, GC Resolv, 4L
Hexane-Burdick & Jackson, GC215-4, Capillary GC/GC-MS Solvent, 4L
Dimethylsulfoxide-Fisher Scientific, D-136, Spectranalyzed, 1L
BSTFA+TMCS 99:1, 20 X 1 mL, Suppelco 33148

8. Safety

- Chemists will wear personal protective equipment (PPE), specifically labcoats, when in the laboratory
- Care should be taken when changing the injector septum. The septum nut is very hot and can cause burns. The GC/MS instrument has many heated zones: the injector, oven, transfer line, source and quadrupole. Routine maintenance requires that these heated zones be cooled prior to handling.
- Always transport helium cylinders secured to a cart. During transport, cylinders must always be capped to protect the shutoff regulator and ensure personal safety.
- Protective eyewear is required when performing maintenance on capillary columns.
- When replacing rough pump fluid, wear appropriate personal protective equipment (PPE): a lab coat, gloves and safety glasses. Used rough pump oil is considered hazardous waste. It will be safely stored in a plastic container until disposed of by the UMASS Environmental Health and Safety Department.
- Use fume hoods when working with solvents.

9. Sample Submission Requirements

A portion of a sample is placed in a vial, either standard or residue sized, dissolved in a solvent, and submitted by the primary chemist to the GC/MS laboratory. All submitted vials will be listed on a Drug Laboratory GC/MS Control Sheet (**Attachment 5**) along with their respective cards. The GC/MS staff will note on the control sheet the day a sample is received along with their initials. All numbered vials are matched against the control sheet and cards prior to acknowledging receipt. If any errors are noted, the entire submission will be returned to the submitting chemist for correction. Samples are also checked for GC/MS suitability. Samples with an excessive amount of particulate matter will be returned. All vials should be legible to the operator. Vials should typically be at least half full and caps should be firmly crimped to avoid evaporation. Samples dissolved in hexane should have new caps as perforated rubber/Teflon septa leach into the solvent.

Samples are then separated into their suspected drug type using separate vial racks: cocaine, heroin, pharmaceuticals, specialties (i.e. LSD, MDMA, THC, Psilocybin, Nitrites, and Alcohols) and unknowns. Analysts submitting pharmaceutical samples should make an effort to cluster as many similar samples as possible on one GC/MS control sheet. First hand knowledge about a samples concentration or cleanliness should be noted on the control sheet by the primary chemist. The GC/MS operator will then choose the appropriate method/QC precautions (blanks) for the item being analyzed.

10. Equipment Maintenance and Calibration/Instrument Quality Control

- The Auto-Liquid Sampler (ALS) rinse bottles must be emptied, washed out and refilled with the appropriate solvent. Waste bottles should be emptied and washed out.
- The injector septum must be replaced on every new run or after approximately 100 injections. Printer paper should be refilled before every new run.
- Injector cleaning and source cleaning procedures can be found on CD. See HP 5973 MSD Disk Reference Collection 1-3 for details.
- On the day a sequence is initiated, perform a PFTBA (perfluorotributylamine) spectrum scan. Check for air leaks. If no air leak is present, perform a Standard Spectra Tune. Tune the instrument on the method that will be used during the sequence. For sequences using multiple methods, load the method with the lowest starting oven temperature and tune on that method. Two operators must check and initial every tune. If the tune is satisfactory, the MS Supervisor or a QC Chemist will fill out the Drug laboratory GC/MS Daily QC Check-**Attachment 6.**

Make sure the following tune parameters are within specified tolerance levels or set properly: mass assignment, unit mass resolution, peak widths, mass 69 abundance, the relative

abundance of 219 and 502, isotope ratios, foreline pressure, source and quadrupole temperatures, electron energy, number of peaks in spectrum scan, air leaks, and relative target abundances of 50,69, 131, 219, 414, and 502. Readings outside the established range should be reported to the MS Supervisor. Note day-to-day trends in the electron multiplier voltage and lens voltages. Report any significant increase/decrease to the MS Supervisor. On the 5973/5975 save tune files to Stune.u and Atune.u on the 5971.

5973/5971	**Relative Ratios for Prominent Masses**		
	5973/5975		**5971**
m/z 69	base peak (100%)	---	base peak (100%)
70/69	> 0.5 but < 1.6 %	---	0.54- 1.6 %
219/69	> 40% but <85 %	---	>30 %
220/219	> 3.2 but < 5.4 %	---	3.2- 5.4 %
502/69	> 2.0 but < 5.0 %	---	>1 %
503/502	> 7.9 but < 12.3 %	---	7.9- 12.3 %
Source temperature: 230 C		---	Determined by the transfer line temperature setting and convection efficiency.
Quadrupole temperature: 150 C		---	Automatically set

- Foreline Pressure: 40-60 mTorr typical. Dependent on the condition of the rough pump. The foreline pressure is adequate under 100 mTorr. The crital foreline pressure is 400 mTorr, above which the diffusion pump and the heated zones turn off. At 300 mTorr, the diffusion pump will turn on during pump down. The MSD manifold vacuum pressure (high vacuum pressure) should be $5X10^{-5}$ torr or lower.
- Electron Energy: 70 eV (69.9 eV)
- Mass 69 abundance: Approximately 200,00 to 400,000
- Mass peak width (PW50) should be 0.55 $\pm$ 0.1 (default) for the 5973/5975 and 0.50 $\pm$ 0.1 for the 5971 MSD.
- Mass assignment is determined on the top portion of the tune. The Drug Laboratory allows masses to vary by $\pm$ 0.1 amu on each tuning mass and isotope mass. Agilent allows $\pm$ 0.2 m/z for 69,219, and 502 on the top and $\pm$ 0.1 m/z on the bottom.
- Note isotope ratio tolerances above. Isotope ratios for 70/69, 220/219 and 503/502 should be close to the theoretical values of 1.08, 4.32, and 10.09. The 69 fragment ions have one carbon atom, the 219's have four and the 502's have nine. The natural abundance of C13 is 1.1%, which explains the observed isotope abundance (1, 4, and 10%) one mass unit away (due to the extra neutron of C13 and N15). Proper isotope ratios can be used to indirectly assess unit mass resolution as can the visual appearance of the profile scan.
- Agilent guarantees that their quadrupole mass analyzer will achieve unit mass resolution throughout the mass range. Unit mass resolution is achieved because peak widths are kept fairly constant throughout the mass range. Using the manufacturer's defined range for peak width (Full Width at Half Maximum-FWHM) ensures unit resolution. Unit resolution means two adjacent peaks in a mass spectrum are resolved

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sufficiently so that the peak height of either peak is not appreciably affected by overlap. In the profile scan of the tune (the top portion showing an extracted ion chromatogram) check that adjacent isotopes are resolved. Historically, the height of the valley between isotope peaks is around 5% or less relative to the larger peak (25% or less relative to the smaller isotope peak). On the bottom part of the tune that shows a full spectrum scan, isotopic masses should also be one mass unit apart $\pm$ 0.2 **u** (unified atomic mass units). If unit mass resolution is not achieved, retune or notify the supervisor for corrective measures.

- Air leaks approaching 10% should be reported. Office Duster can be used to determine the source of the leak by acquiring spectrum scans under Diagnostics/Vacuum Control. On the 5971 MSD, an air and water check will give relative abundance for water (mass 18), nitrogen (mass 28), oxygen (mass 32), and carbon dioxide (mass 44). The 5973/5975 MSD will give the relative abundance of water and nitrogen. Oxygen and carbon dioxide can be approximated from the graphical output. If an air leak is present, the ratio of m/z 28 to m/z 32 will be about 5:1.
- Electron multiplier voltage (EMV) should be less than 2500. 3000 is the upper maximum. Notify the supervisor if the EMV is above 2500.
- The relative target abundance (on the 5973/5975 MSD) for mass 50,131,219,414, and 502 are set at 1,55,45,3.5, and 2.5. The 5971 MSD does not give operators access to these parameters.
- The full spectrum scan should contain < 200 peaks (typically 80-150). Report tunes with an uncharacteristically high number of peaks. See **Attachment 7** for a list of contaminants and their possible source of origin.
- Operators on the 5973/5975 may perform a system verification tune if questions arise about the status of the MSD. This evaluation allows the analyst to check the MSD using a maximum sensitivity tune (maximizes the abundance of tuning mass 69,219 and 502) and not a standard spectra tune. It will not verify if the last standard spectra tune passed all Drug Laboratory standards but it can serve as a good diagnostic tool.
- **Individuals who make use of the equipment are responsible for determining whether or not the instrument has been qualified for operation. Instrument quality control (MSD tune, injector/column QC) and method quality control (blanks and standards) are the determining factors for use.**

GC/MS Standard Spectra Autotune (Target Tune) Checklist

Correct Mass assignment in profile scan and spectrum scan
Peak widths
EMVolts
Source Temperature

Quadrupole Temperature
Foreline Pressure (5971, 5973) or High Vacuum Pressure (5975) and Turbo Speed
Electron Energy
Number of peaks in spectrum scan
Unit mass resolution
Isotope Ratio (Resolution of profile scan should corroborate isotope ratios)
Mass 69 abundance
Relative abundance of 219
Relative abundance of 502
Air leaks
Target Abundance (1.0, 100.0, 55.0, 45.0, 3.5, 2.5)

11. Batch Setup-Procedures and Method Quality Control

Samples are always bracketed by standards. Bracketing standards are used after every tenth item when possible. Plus or minus a few vials is acceptable. This ensures the instrument is operating properly at the beginning, middle and end of the sequence with respect to retention time and spectrum. If the instrument malfunctions at the very end of a sequence, the majority of the samples can be analyzed up to the last satisfactory bracketing standard.

Operators must insure carry-over does not exist between samples or between a standard and the next sample. This is accomplished by running blanks (the solvent that the sample is dissolved in) between all vials, both standards and samples. Fresh blanks should be made up with every new run to avoid septum leaching. Two full blanks typically will suffice for a full tray of samples. The first blank will be used for the first half of the run and the second blank will be used for the second half of the run. Standards should be recapped after one or two uses to prevent septum contamination. If a standard completely breaks down or if breakdown products account for more than 25-30% of the standard's area, that qualitative standards should be discarded. Exceptions include standards known to be thermally unstable or a mixture of cis/trans isomers exist. Reactive solvents will only be used if no other solvent is suitable. When the last standard is discarded, QC should be informed to prepare new standards. See **Attachment 8** for standard QC procedures.

The Drug Laboratory Batch Sequence Sheet **(Attachment 9)** is filled out using blanks after every sample and standard. In the case of a multiple, a blank must be inserted after every fifth specimen vial. If a submission is not an even multiple of five, blanks can be inserted more or less to evenly divide the case. For example, a case with eight specimens can be divided up four and four. There are times when double blanking may be useful. For example, carry-over may be more likely to occur at the beginning of a sequence or when a sample is known to be very concentrated. Double blanking for pharmaceutical drugs is highly recommended, as are drugs that originate from natural products (i.e., psilocybin mushrooms).

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A QC standard mix comprised of cocaine and codeine is placed at the beginning of every sequence. The acquisition method must always be DRUGS.M. It will be used to monitor the status of the column and the general cleanliness of the injector. The retention time ratio of codeine/cocaine is determined to assure the column is capable of separating components of a mixture. The abundance of each peak can be used to gain insight to problems that may exist with the injector and even with the column/source.

After the sequence for the batch sheet is determined, operators need to fill out the top of the form by noting the setup date, the setup analyst, the data file range of numbers to be used, and the sequence name for the run. The sequence name is the day of the run preceded by the instrument's assigned letter (i.e. E102402.s for system 5). When the sequence is typed into Chemstation, individual numerical data files are organized in Window's Explorer using the date with underscores (i.e. 10_24_02 may have data files 598,001-598,099). The sequence file name and the organizing data file name should share the same date. This date should also match the date on the tune. The sequence is saved and a hard copy is printed.

After the sequence is started, it is the operator's responsibility to make sure both the first blank and QC Test Mix are satisfactorily. Operators need to complete the GC/MS Daily Injector/Column Check sheet **(Attachment 10)** so the MS Supervisor/QC Chemist can fill out the Drug Laboratory GC/MS Daily QC Check sheet. If the laboratory's QC parameters fail, the run should be aborted or reported to a supervisor. A multitude of malfunctions can occur at the beginning of a sequence and the operator should check the instrument repeatedly throughout the day. If the system malfunctions at the beginning of a sequence, resume the instrument if possible. Otherwise, notify the MS Supervisor. If the problem is not addressed until the next day, re-tune the MSD. Make appropriate changes to the sequence file name, the data file path and to the data file book. If the system malfunctions at the end of the sequence, restart the instrument to finish the sequence. Retune the instrument if the malfunction occurred over the weekend (> 48 hrs) and save it with the original tune. Note on the sequence sheet where retuning occurred. If the instrument is inoperable, samples can be analyzed up to the last completed bracketing standard. For QC reasons, operators should save the hand written sequence sheet even if a sequence is completely aborted and no analytical data is used for confirmatory work. Operators should add a simple note explaining what happened to the samples of an aborted run. For example, samples could be placed on a different sequence or put back on the shelf.

Miscellaneous
-Avoid dividing a case's samples among different operators. This will minimize the possibility of several chemists having to appear in court.

- Operators should re-check that the laboratory numbers on the GC/MS control sheet match the numbers on the vials and card.

-Check the GC/MS control sheet for special instructions advising the operator to use a specific method. Standards, samples and blanks should be analyzed using the same method. For very weak samples, a modified method incorporating a lower split ratio and a higher electron multiplier voltage may be used with all other parameters remaining constant. The preceding blank should also be acquired on the more sensitive method as well.

-The GC/MS Laboratory will routinely confirm the highest class drug in a sample.

-Available methods-See Attachment 11 for Method Parameters
Alcohol.m
Clonaz.m
Drugs.m
Genscn.m
GhB.m
Lsd.m
Mdma.m
Mush.m
NaSalt.m
Nitrites.m
Screen.m
Speed.m
Viagra.m
Thc.m

More Sensitive Methods for Weak Samples/Standards
W/Pthc.m
W/Pdrugs.m
W/PClonaz.m
W/PGenscn.m
W/PGhb.m
W/PMdma.m
W/PMush.m

W/PScreen.m
W/PSpeed.m

Methods with a P prefix indicate a pulsed method for greater sensitivity than W (weak) methods.

12. Analytical Interpretation

Operators are expected to analyze data results by comparing the sample data to an authentic standard. A positive identification is made when the unknown and standard have consistent retention times (within +/- 1.5 % of the standard) and mass spectral fragmentation patterns (acquired in full spectrum scan mode).

Positive Confirmation-Match quality, as seen on every report, is only used as an interpretative guide to an unknown's identity and is not the determining factor for a positive identification. **All confirmations are always made by the analyst, not the instrument**. **Identification is based on corroborating results which include retention time, unique ions (ion clusters), ion abundance, literature reference comparison, probability based matching scores, method QC controls and preliminary findings**.

Minimum Acceptance Criteria for Mass Spectral Confirmation- A critical responsibility of every operator is to determine when the analyte concentration is high enough to positively confirm its presence in a sample. Concentration plays a crucial role in qualitative identification. It not only determines relative abundance but also which ion masses are present or absent. The end result of all GC/MS data, whether it is a standard or a sample, must be to yield a searchable spectrum. The operator does not rely on the instrument for the answer to this question via match quality. Match quality alone can lead to misidentification as well as under-identification. Instead, the operator must rely on an accepted spectrum from a published reference book or library. The minimum abundance for a particular analyte is achieved when it can be matched to a reference spectrum. This rule will apply to sample confirmation work and standard QC work performed by the laboratory. To obtain the necessary detail in a spectrum, the operator has many options available. A sample can be physically concentrated or it can be run on a more sensitive method. No general tolerance level for relative abundance will be stated. The exact definition of standard spectra tune is quite broad and not all reference spectra were acquired on the same type of instrument. (Some spectra were obtained using direct insertion probes at high temperatures.) Relative abundance will be left to the operator's discretion when a reference spectrum is being compared to a standard or sample. However, for a standard and sample being analyzed on the same instrument the relative abundances should mirror one another. Only differences in concentration can explain differences in relative abundance/match qualities.

Carryover- No carryover of the controlled target compound is allowed in the blank before a sample. Carryover is present when it is visible above the general noise level. When a defined

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peak begins to appear in a blank at a compound's retention time, even under 2 times the noise level, the operator must check if this is carryover. If ions of the target compound are present, carryover is present. Carryover after a multiple requires that the multiple be repeated and also the next sample (if one is present). Carryover after a multiple raises the possibility that carryover occurred during the multiple. Ghost peaks, when identical to the target compound at a different retention time, are not allowed. Please bring ghost peaks to the attention of the GC/MS Supervisor. A late eluter, such as noscapine in heroin, is acceptable since it can be explained.

Occasionally an unknown may have a peak of interest that does not integrate. If the peak area of the TIC is below 100000, no report will be printed for this peak. One approach to non-integrated peaks involves using data analysis to manually analyze and print the results. Another approach is to lower the method's integration area threshold. If the analyte in question is too weak (does not meet minimum spectral requirements), the sample will need to be re-analyzed. The operator has the option of re-analyzing the sample on a more sensitive GC-MS method or, if necessary, it can be returned to the primary chemist for concentration. Once resubmitted, it can be re-analyzed on the same or more sensitive method depending on the situation. When screening an unknown, all non-integrated peaks must be checked for controlled substances.

In the event GC/MS results are out of character with preliminary results, consult the primary chemist. A second analysis may be necessary to rule out initial inconsistencies that may exist. All negative samples should also be returned to the primary analyst if additional testing is required. All unknowns found to contain a controlled substance must also be returned to the primary chemist for final confirmation.

Use of Background Subtraction-Just like relatively constant noise from column bleed can be removed from a peak, background subtraction can be used when compounds elute in close proximity to one another. When compounds are separated by some amount of time, operators can successfully subtract unwanted ions. However, operators will not find this technique of assistance when compounds co-elute at the exact same moment in time. If co-eluting peaks share common ions, background subtraction will be problematic and confirmations may not be possible.

Fronting- The reported mass spectrum for each peak is generated using an apex minus start of peak background subtraction technique. For peaks that front, the true spectrum is not represented in the report and the operator should manually integrate these peaks. For weak samples, the operator can subtract ions at the end of the peak to remove background noise.

Identification of Unknowns- Unknown items are to be analyzed using the screen method. When screening unknowns all integrated and non-integrated peaks must be checked for controlled substances. Screen is designed for early and late eluters. The only exception to date is Sildenafil (Viagra). It will appear in the following blank so operators must end all unknown runs with a blank. The chromatography for screening may not be optimized for every drug but

the spectral results should be adequate for identification. Once an unknown is preliminarily identified, confirmation is performed with bracketing standards using an appropriate method determined by QC. Tailored methods exist to improve chromatography and shorten run times when possible.

Library search results use a combination of common names and chemical names. If a chemical name is used the operator can find a list of synonyms in Nist Output or by doing a Nist search. Once the common name for a compound is determined, the GC/MS operator must determine if it is a controlled substance. The operator will use a combination of resources to determine the legal status of a drug including the Physicians' Desk Reference, Massachusetts General Law, Chapter 94, Section 31 for the Controlled Substance Act, **Attachment 12**, the Microgram Bulletin, Volume XXXVIII, No. 5, May 2005 which summarizes the 59 controlled steroids in the Federal Anabolic Steroid Control Act of 2004, Public Law 108-358, and the US Drug Enforcement Administration Drug Scheduling List, **Attachment 13.**

The above training instructions may not handle every possible working situation. Any doubts or questions should be taken to a senior chemist or supervisor. It is a requirement of the job and an expectation of the laboratory

13. Limitations of GC/MS

- Compounds must be volatilized by the GC
- Sensitive to active sites -Affects sensitivity and carryover
- Thermal Breakdown
- Chemical reaction with the solvent in the injection port.
- Will not determine salt forms or distinguish between enantiomers
- Identification of unknowns limited by libraries and reference books
- Library match quality not always accurate due to concentration
- Operators unfamiliar with the GC-MS analysis of a certain drug should check the standard QC folder for the proper method of analysis.

14. Test Reporting

All results will be reported on the GC/MS Control Sheet and the sample card assigned to every case. On the top of the control sheet, next to date analyzed, the operator needs to place the date the run was analyzed (the day the chemist sits down and reviews the results) and the sequence file name for retrieval purposes. If a sample needs to be returned to the primary chemist for

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additional testing, the date analyzed for the control sheet remains the **GC/MS analysis date**. The primary chemist will write on the front of the card their analysis date for when he/she completes the analysis. Fill out the remainder of the sheet by noting the retention times of the bracketing standards (under MS comments), the operator initials (under MS BY), the retention time of the unknown and the match quality (under RT/MQ), and lastly the findings under results.

Under the comment section of the GC/MS control sheet, GC/MS analysts may also note any other controlled substance of a similar or lower class. These findings will not be reported on the certificate but making note of them can be helpful. If more than one controlled substance of an equal class is present, the stronger or more prominent peak is usually identified. Occasionally more than one controlled substance is reported, in which case the appropriate standards are used (i.e. mixtures of ketamine and ecstasy or methamphetamine).

The front of the sample card is filled out noting the date analyzed (upper right hand corner), the number of tests performed plus initials by the GC/MS operator (gas chromatography counts as one test and mass spectrometry as another) and the finding. The operator should place a red dot next to his/her initials in order to be identified as the secondary chemist. On the back of the card the operator notes if the GC/MS was positive/negative and the sequence file name. One must also write in the results and the analysis date here if the finding/analysis date is not reported on the front. For example, the card needs to be returned for crystal tests, THC quantification, ketamine salt form determination, or additional GC testing.

Completed cards are returned to the evidence office to generate certificates. All GC-MS analytical hardcopies are saved. The original copy of the tune report stays in the GC/MS Laboratory for QC purposes. A second copy of the tune report stays with the instrument hardcopy. A copy of the sequence batch sheet stays in the GC/MS Laboratory. Two copies of the GC/MS control sheet need to be saved: one for the GC/MS Laboratory and the original should be returned to the primary chemist. Data can be retrieved from the hardcopies or from the backup/archive compact discs.

15. Data Storage and Retrieval

Two copies of digital data should exist at all times, one on the acquiring instrument and one on the stand-alone computer. Data backup should be performed as soon as the run is complete or immediately after it is analyzed. Hitting the data backup icon on the 5973/5975 instruments or the compact disc icon on the 5971 performs data backup of the completed sequence. Before initiating data backup, the operator should be certain transcriptional errors do not exist. Proofreading, double-checking, etc should be performed before the sequence is initiated and at the very least when the run is completed. Address transcriptional errors with the MS Supervisor or simply make personal notations on all applicable paperwork. At the end of every month, the GC/MS Laboratory will store all analytical results on recordable compact discs (CD-R). Two CD-R copies are created: a

backup copy and an archive copy. Raw data on the stand-alone computer is erased after duplicate CDs are created.

Data can be retrieved from the hardcopies or from the backup/archive compact discs. Electronic retrieval is only possible from the 5973/5975 instruments (systems 4, 5, 6 and 7) under Data Analysis. Not all the instruments have the same libraries. Therefore, reprocessing should be performed on the instrument the data was acquired on with the proper acquisition method loaded. The only way to get a duplicate copy from system 3 is from the hardcopy. Otherwise, the raw data can be reprocessed on the 5973/5975 instruments but the match qualities may be slightly different. For discovery motions, supply bracketing standards, the sample(s) and blanks. Blanks should include those preceding the unknown and the bracketing standards.

16. Record Retention

GC-MS hardcopies, the backup CD/DVD and the archive CD/DVD are to be safely stored for a period of 15 years from the date of analysis. The equipment and software needed to open the raw data files also needs to be kept for the same period of time. In the event of a fire, CD/DVD copies should be stored in separate locations.

16. Compliance Monitoring

Monthly QC sample audits will examine GC-MS results to ensure this SOP is being followed. The GC/MS Supervisor will perform the audit.

17. References

Hewlett Packard
HP GC-MSD Chemstation and Instrument Operation- Student Manual
Volume 1 and Volume 2
G1701BA Version B.01.00
Course Number H4043A

HP 5973 MSD Reference Collection
Disc 1/3
Reversion C.00.00
February 1998

Hewlett Packard
Hp 5973 Mass Selective Detector Hardware Manual, Manual Part # G1099-90001
First Edition, 8/96

Hewlett Packard
HP 5971A MSD Hardware Manual, Manual Part # 05971-90019
Third Edition
Copyright 1991

Hewlett Packard
HP G1034C
MS ChemStation Software User's Guide, Manual Part #G1034-90043
Copyright 1993
First Edition

Mass Spectrometry Desk Reference
First Edition
O. David Sparkman
Global View Publishing
Copyright 2000

Analytical Chemistry
Fourth Edition
Gary D. Christian
Copyright 1986 by John Wiley & Sons, Inc.

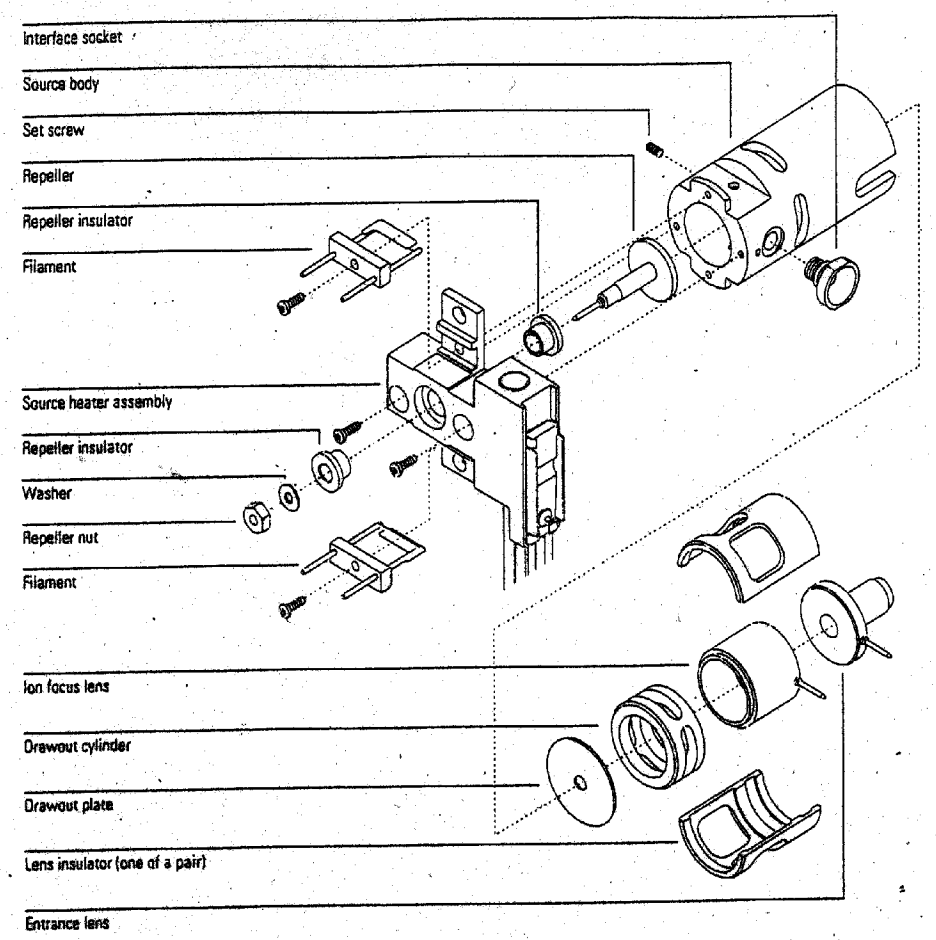
Introduction to Organic Laboratory Techniques- A Contemporary Approach
Pavia, Lampman and Kriz-Western Washington University
Second Edition
CBS College Publishing, Copyright 1982
Practical Quadrupole Theory:Graphical Theory
Randell E. Pedder
ABB Inc., Analytical-QMS Extrel Quadrupole Mass Spectrometry
575 Epsilon Drive
Pittsburgh, PA 15238

18. Attachments

Attachment 1A- Ion Source Breakdown
Attachment 1B-The Mathieu Stability Diagram
Attachment 2-Practical Quadrupole Theory:Graphical Theory
Attachment 3-HED/EM Functional Diagram

Attachment 4-Drug Laboratory GC-MS Standards
Attachment 5-Drug Laboratory GC-MS Control Sheet
Attachment 6-Drug laboratory GC/MS Daily QC Check
Attachment 7-Common Contaminants
Attachment 8-Standard Preparation QC Procedures
Attachment 9-Drug Laboratory Batch Sequence Sheet
Attachment 10-GC-MS Daily Injector/Column Check
Attachment 11-GC-MS Methods
Attachment 12-Microgram Bulletin,Volume XXXVIII, NO. 5, May 2005
Attachment 13-DEA List of Federally Scheduled Controlled Substances

Attachment 1A



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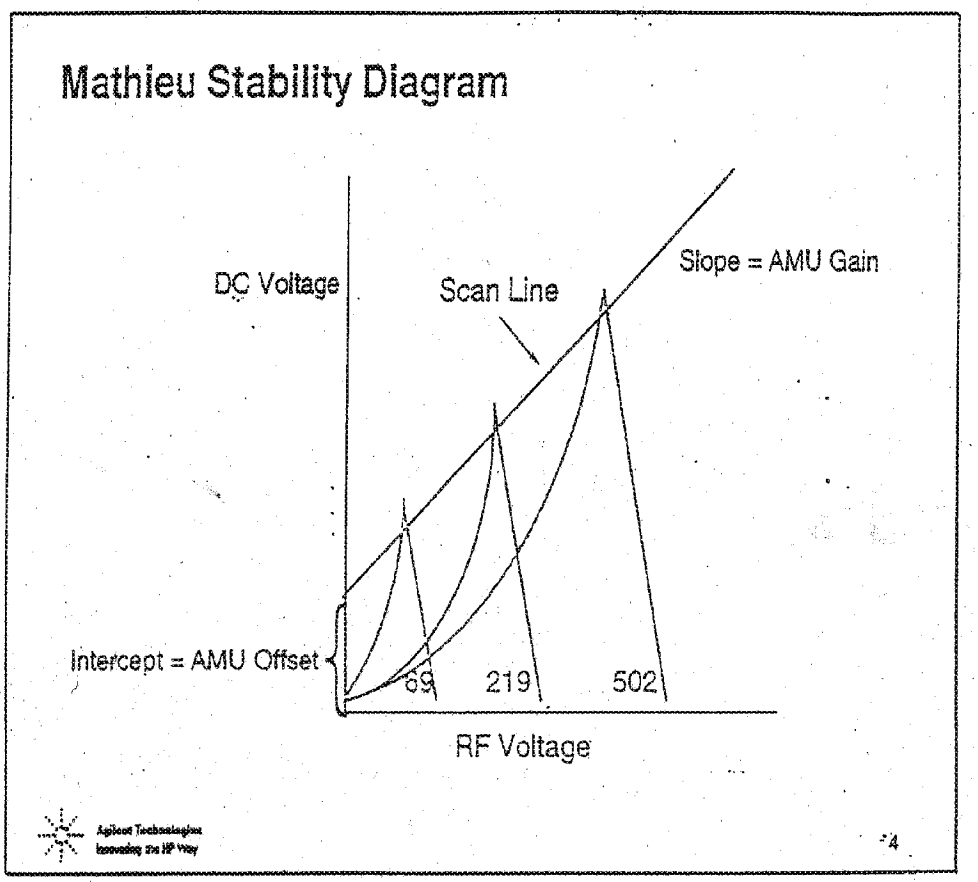
Attachment 1B

Mathieu Stability Diagram



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Attachment 2

Extrel Application Note RA_2010A

Practical Quadrupole Theory: Graphical Theory

Randall E. Pedder
ABB Inc., Analytical-QMS Extrel Quadrupole Mass Spectrometry, 575 Epsilon Drive, Pittsburgh, PA 15238

(Poster presented at the 49th ASMS Conference on Mass Spectrometry and Allied Topics, May 28 - June 1, 2001)

Traditional treatments of how quadrupoles work rely heavily on complex equations, both empirically and analytically derived. Newcomers to the field are often overwhelmed by the abstract nature of such purely theoretical treatments, often requiring in depth study to reach an intuitive understanding of how quadrupoles work, and more importantly, how to optimize performance in experiments involving quadrupoles.

This presentation focuses on the use of graphical tools to provide an intuitive understanding of how quadrupoles work. The correlation between the Mathieu stability diagram and peak width and mass calibration is illustrated. Voltage scan lines through the regions of stability for the stability diagram are correlated with mass peak widths. Changes in the intercept and slope of the scan line are demonstrated for use to control peak width, to approximate unit mass resolution across the mass range. Once the basic graphical concepts presented here are mastered, the reader is directed to review a more rigorous treatment of quadrupole theory such as the most excellent treatment found in the second chapter of March and Hughes' book "Quadrupole Storage Mass Spectrometry".(1) The second chapter is titled "Theory of Quadrupole Mass Spectrometry" and provides a quite approachable introduction to the equations and their derivations. Of course, the most rigorous treatment of quadrupole theory is present in Peter Dawson's classic "Quadrupole Mass Spectrometry and its Applications".(2) That book and subsequent papers by Dawson are thorough in their coverage, and are quite approachable once one has developed an intuitive understanding of the basic concepts.

This presentation approach is unique to any yet found in the literature, with its focus on practical implications of quadrupole theory, de-emphasizing the complex abstract equations typically utilized in traditional summaries of quadrupole theory.

I. INTRODUCTION

The purpose of this presentation is to de-mystify the theory associated with how quadrupoles operate.

This introduction is a collection of general background information intended to clarify the typical implementations of quadrupole systems.

A quadrupole mass filter consists of four mutually parallel, high mechanical precision, electrically isolated electrodes oriented such that the electric field between them is hyperbolic (quadrupolar).

While some manufacturers choose to fabricate high precision hyperbolic surfaced electrodes, a common way to manufacture a quadrupole is to orient four round poles such that their centers coincide with the corners of an imaginary square.

The round poles would be oriented such that the distance between the faces of opposite poles is nominally 1/1.148 times the rod diameter. This ratio is chosen such that the geometric center of the quadrupole approximates an ideal hyperbolic field.

Ions to be mass analyzed are focused down the center of the quadrupole, with a combination of precise DC and RF voltages applied to the quadrupole rods (typically a constant RF frequency, 700 kHz to a few MHz).

For a given system, the amplitude of the voltages determines which mass (or range of masses) will have stable trajectories through the quadrupole. Ions having unstable trajectories are neutralized by striking the quadrupole electrodes.

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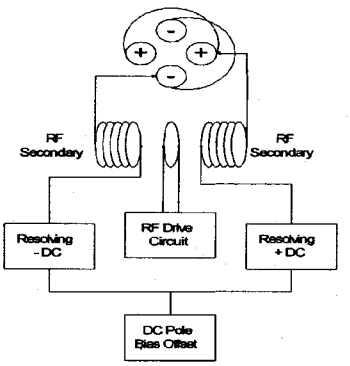

Figure 1. Schematic of typical quadrupole power supply connections.

Opposite pairs of quadrupole rods are typically electrically connected, yielding a requirement for two electrical connections to the quadrupole.

The quadrupole power supply can be schematically described to include:

- A DC pole bias supply which determines the centerline potential of the quadrupole (i.e. same potential and polarity added to both pairs of rods).
- Two Resolving DC supplies providing equal magnitude but opposite polarities to each pair of quadrupole rods. The potential for both of these DC supplies are biased from ground by the pole bias supply.
- A high voltage RF transformer circuit which has a single primary and two secondaries, which are 180 degrees out of phase with each other. The resolving DC supplies serve as inputs to the secondaries.

II. SOLVING THE EQUATIONS

Don't read this section! It is obligatory that any presentation about quadrupole theory has to at least mention the Mathieu equation. **Skip over to the section entitled "Graphing the Solution ".**

The traditional treatment of quadrupole theory starts with a derivation of the Mathieu equation from 'F=ma' all the way through to the final parameterized form, with the following parametric substitutions:

$$\frac{d^2u}{d\xi^2} + (a_u - 2q_u \cos 2\xi)u = 0 \qquad a_u = \frac{8eU}{mr_0^2\Omega^2} \qquad q_u = \frac{4eV}{mr_0^2\Omega^2}$$

The u in the above equations represents position along the coordinate axes (x or y), x is a parameter representing Wt/2, t is time, e is the charge on an electron, U is applied DC voltage, V is the applied zero-to-peak RF voltage, m is the mass of the ion, r is the effective radius between electrodes, and W is the applied RF frequency.

The rigorous analytical solution to this second order linear differential equation is:

$$u(\xi) = \Gamma \sum_{n=-\infty}^{\infty} C_{2n} \exp(2n+\beta)i\xi + \Gamma' \sum_{n=-\infty}^{\infty} c_{2n} \exp-(2n+\beta)i\xi$$

Which, intuitively obvious to any person skilled in the art, reduces to a similar infinite sum of sine and cosine functions. But for our purposes, it is acceptable to simply consider ion trajectories to be infinite sums of sine and cosine functions, with each successive term having smaller amplitude and higher frequency.

Which really means that motion in each of the x and y directions is sinusoidal, consisting of macromotion at the fundamental frequency (ω_0), with micromotion at the harmonic frequencies added in, (or if the fundamental and the first harmonic are close in frequency, a beat pattern of the fundamental and the first harmonic, with micromotion of the rest of the harmonic frequencies added in).

III. GRAPHING THE SOLUTION...

But what really matters rather than the exact solutions of the Mathieu equation is: **Does the ion have a stable trajectory at the voltages applied? (i.e. Will the ion go through the quadrupole?)**

The answer to this question can be readily treated graphically. Simply plot the families of solutions to the Mathieu equation that have stable trajectories, and look to see if the voltages in question lie inside or outside one of the stability regions defined by the Mathieu equation solution boundaries.

Figure 2 (adapted from Figure 2.7 of Reference 1) shows the families of solution boundaries for the Mathieu equation that lie near the origin, showing four distinct regions of stable trajectories (with boundaries for both the x and y directions plotted) for ions moving through the quadrupole, using the Mathieu a and q parameters.

Region A from Figure 2 represents the traditional operating region for quadrupole mass filters. Figure 3 is an amplified view of this *First Stability Region*, with

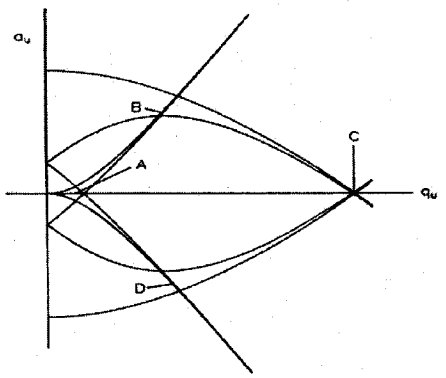

Figure 2. The Mathieu stability diagram in two dimensions (x and y). Regions of simultaneous overlap are labeled *A*, *B*, *C*, and *D*. [1]

suitable substitutions for the Mathieu parameters a and q to convert the axes into RF-DC voltage space for m/z 219, with r_0 calculated based on a 9.5 mm round quadrupole rod diameter, and an operating frequency Ω of 1.2 MHz.

For any set of RF and DC voltages, one could read directly from this figure whether ions of m/z 219 would have stable trajectories through a 9.5 mm quadrupole operated at 1.2 MHz. The area inside the boundaries represent voltages with stable trajectories, and the area outside the boundaries represent unstable trajectories for that stability region.

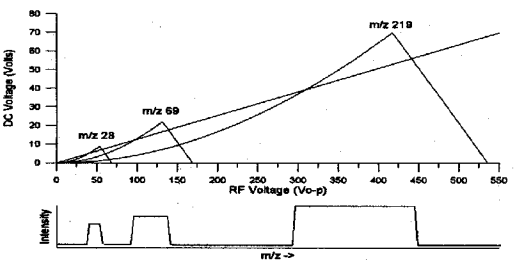

Figure 4. Stability diagrams for m/z 28, 69 and 219 plotted in RF-DC space, showing a straight scan line through the origin. The lower portion of the figure represents the mass peak widths resulting from the scan line passing into and out of the stability regions for each of the masses.

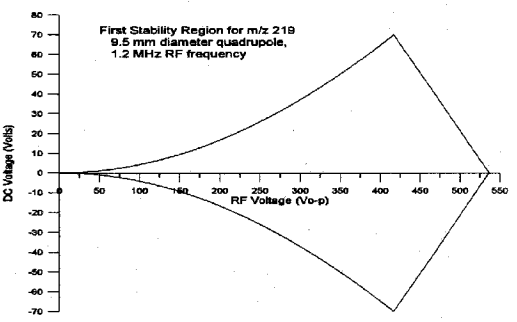

Figure 3. Expanded view of region *A* from Figure 2 (the '*First Stability Region*') with suitable substitutions for a and q to convert into RF and DC space for mass 219 for a 9.5 mm quadrupole operated at 1.2 MHz.

IV. CONSTANT RESOLUTION SCANS

Note that the stability diagram shown in Figure 3 is symmetric around the DC voltage = 0 axis. In practice, when one assigns positive DC voltages to one rod pair, and negative DC voltages to the other pair, only the top half of this diagram is considered, with the bottom half of the diagram accessible by simply swapping the electrical connections to the quadrupole.

Figure 4 represents the stability diagrams for multiple masses plotted in the same RF-DC space. A linear scan line is drawn from the origin through the stability regions, passing from instability to stability back to instability for each of the masses. The bottom portion of Figure 4 represents the ion current that would be measured if RF and DC voltages are scanned through the values along this scan line as a function of time. If ions of various masses are directed into the quadrupole entrance, only certain ions will pass through the quadrupole to a detector at the exit, depending on whether the voltages yield stable trajectories. The various mass peak widths and positions correlate to the boundaries of their associated stability diagrams.

With a linear scan line through the origin, peak widths increase geometrically with increasing mass! (constant resolution)

If the slope of the mass scan line is decreased (dotted scan line in Figure 5), the scan line passes through a wider portion of the stability diagram, effectively widening the mass peak.

Note that the leading edge of the stability diagram comes up three times more slowly than the trailing edge goes down. The net result of this characteristic shape

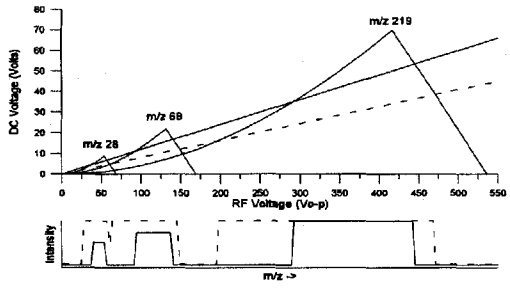

Figure 5. When the slope of the scan line is reduced (dotted scan line through the stability diagrams), the mass peaks widen, with the center of mass position moving to lower apparent mass.

of the stability diagram is that as the resolution is decreased (making the peak wider) the location of the leading edge of the mass peak moves to lower apparent mass three times faster than the trailing edge of the mass peak moves to higher apparent mass, yielding a shift of the center of the mass peak to lower apparent mass.

Changes to Mass Resolution result in predictable changes in Mass Calibration!

V. UNIT MASS RESOLUTION SCANS

Traditional treatments of quadrupole theory, including references 1 and 2 generally suggest that the typical quadrupole scan line is one with a constant *a/q* ratio (i.e. scan line drawn through the origin with constant slope in RF-DC space yielding constant mass

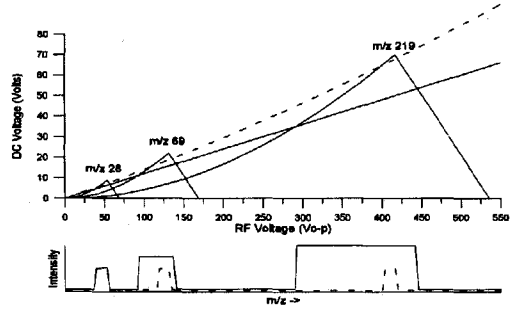

Figure 7. In order to achieve constant peak width across the mass range, a scan line that goes through the origin must be a curve with an increase in the DC to RF voltage ratio with increasing mass (dotted line in figure above).

resolution).

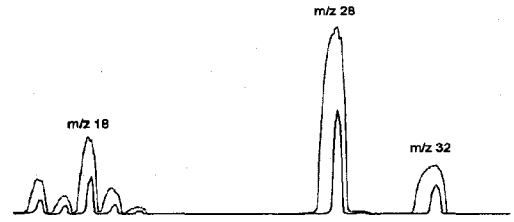

Figure 6. Experimental mass scan from m/z 15 to 35 demonstrating two different mass resolutions. Note that the scan showing wider peaks (red line) demonstrate lower apparent mass positions than the narrower mass peaks, as predicted by theory. These spectra were acquired using the Extrel Merlin Automation data system, and were gathered using a 19 mm tri-filter quadrupole operated at 1.2 MHz.

Commercial quadrupoles are almost **never** operated in this constant resolution mode, rather they are generally operated with a mass resolution that increases linearly with increasing mass (i.e. constant peak width, or Unit Mass Resolution).

To achieve unit mass resolution across the mass range, a scan line that goes through the origin must be a curve with an increase in the DC to RF voltage ratio with increasing mass. (See Figure 7.)

Historically, this curved ideal scan line has been approximated using a straight line in analog hardware by raising the slope of the scan line and lowering its intercept so as to not go through the origin. (See Figure 8). The intercept and slope are generally set empirically by simultaneously optimizing light and heavy calibration masses to unit mass resolution. Unfortunately, masses between these endpoint masses will not have constant peak width using a straight scan line.

In Extrel systems, the intercept, which primarily affects low mass resolution, is called delta-M, and the slope of the scan line, which primarily effects high mass resolution, is called delta-Res. This nomenclature is rumored to be taken from a paper or report published in the early 1960 s by someone at MIT???

The 'error function' that represents the difference between the straight line approximation and the 'ideal' curved scan function (see Figure 9) has been implemented in commercial systems both in analog electronic circuitry and in software.

Extrel traditionally calls such an analog correction circuit the 'linearizer' circuit. Other manufacturers are rumored to have similar circuits in their designs.

VI. CONCLUSIONS

The purpose of this presentation is to de-mystify the theory associated with how quadrupoles operate.

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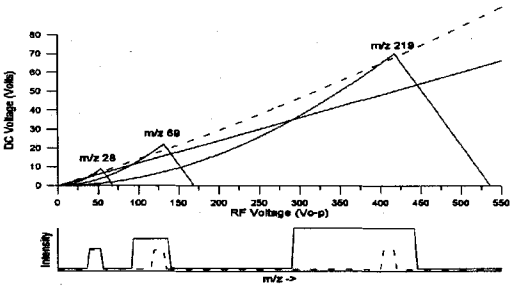

Figure 8. In order to achieve constant peak width across the mass range, a scan line that goes through the origin must be a curve with an increase in the DC to RF voltage ratio with increasing mass (dotted line in figure above).

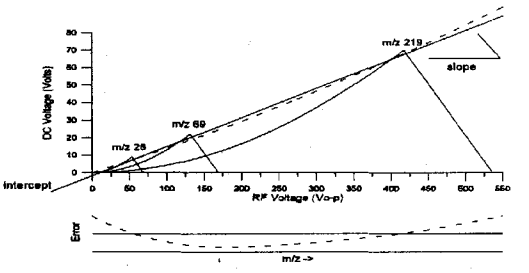

Figure 9. The 'error function' that represents the difference between the straight line approximation and the 'ideal' curved scan function has been implemented in commercial systems both in analog electronic circuitry and in software.

Using this graphical approach, quadrupole operation can be understood intuitively without extensive study of the equations of motion.

A quadrupole operates as a band-pass filter with stable transmission dictated for a given ion by its mass-to-charge ratio and whether the applied RF and DC voltages fall within the stability diagram for that mass-to-charge.

The mass resolution for a quadrupole is controlled via the application of a certain ratio of DC and RF voltages. Increasing the DC to RF voltage ratio will increase mass resolution to the extreme that the DC-RF operating points lie outside the stability diagrams. (i.e. above the apex of the stability diagram, with the apex representing infinite resolution).

With a linear scan line through the origin, peak widths increase geometrically with increasing mass! (constant resolution)

Changes to Mass Resolution result in predictable changes in Mass Calibration. Decrease resolution to make the mass peaks wider and the center of the mass peaks will move to lower apparent mass.

Traditional summaries of quadrupole theory mislead the reader into believing that quadrupoles are operated with constant *a/q* ratios (Constant DC to RF voltage ratios), and hence constant resolution.

Commercial quadrupoles generally use some electronic or software implementation to approximate the curved scan function defined by physics to yield unit mass resolution.

VII. REFERENCES

1. March, R.E., and Hughes, R.J. *Quadrupole Storage Mass Spectrometry*, Wiley Interscience, New York, 1989. Chapter 2: "Theory of Quadrupole Mass Spectrometry", Pages 31-110.
2. Dawson, P.H. *Quadrupole Mass Spectrometry and its Applications*, Elsevier, Amsterdam, 1976.

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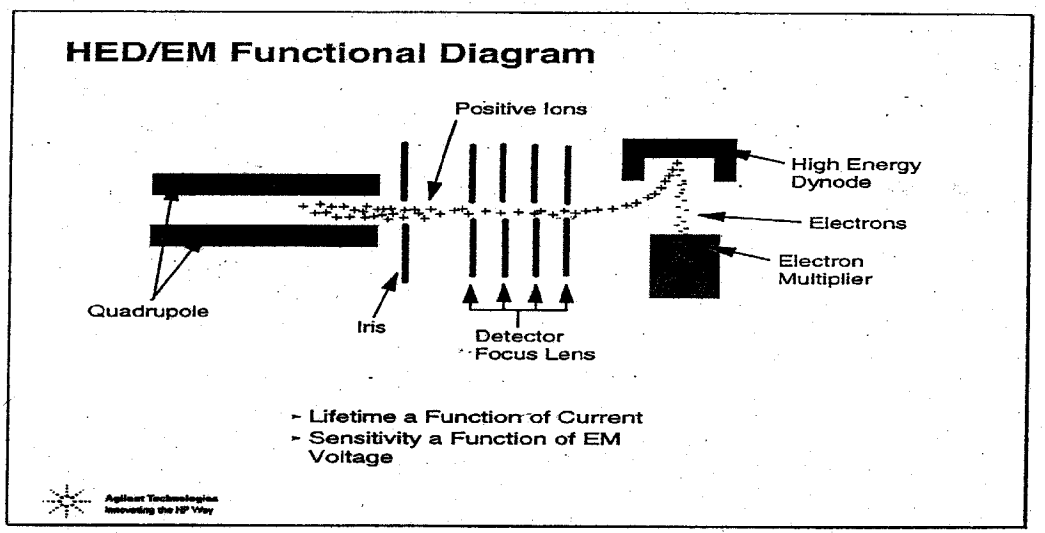
Attachment 3



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Attachment 4

1,4-BUTANEDIOL/MS-241 ALDRICH 240559
2,3-MDA HCL/MS-133
2,3-MDMA/MS-116
3,4-MDA HCL/MS-92
3,4-MDMA HCL/MS-91
4-BROMO-2,5-DIMETHOXYAMPHETAMINE/MS-255
ACETAMINOPHEN/MS-58
ACETOPROMAZINE/MS-230
ACETYLCODEINE-6/MS-142
ALBUTEROL/MS-20
ALFENTANIL/MS-104
ALLOPURINOL/MS-287
ALPHENAL/MS-46
ALPRAZOLAM/MS-30 CONSUMED CBS STANDARD AVAILABLE
AMITRIPTYLINE HCL/MS-29
AMLODIPINE BESYLATE/MS-198
AMOBARBITAL/MS-98
AMOXAPINE/MS-48
AMPHETAMINE HCL (L)/MS-139
ANASTROZOLE/MS-245 LOT LJ0083 CONTROL
ANDROSTENEDIOL/MS-210
ANTIPYRINE/MS-179
ARECOLINE HBR/MS-231
ASPIRIN/ MS-4
ATENOLOL/MS-232
BARBITAL/MS-55
BENZOCAINE/MS-94
BENZOIC ACID/MS-43
BENZONATATE/MS-201
BENZOYLECGONINE TETRAHYDRATE/MS-11
BENZPHETAMINE HCL/MS-27
BENZTROPINE MESYLATE/MS-223
BENZYLPIPERAZINE/MS-268 1.0 MG/ML IN METHANOL
BOLANDIOL / MS-246
BOLDENONE UNDECLCLENATE/MS-172 REFRIGERATOR
BOLDENONE/MS-69
BROMAZEPAM/MS-196
BROMOCRIPTINE MESYLATE/ MS-32 CONTROL
BUFOTENINE MONOOXALATE/MS-128
BUPIVACAINE HYDROCHLORIDE/MS-281
BUPRENORPHINE HCL/MS-136 CLASS E
BUPROPION/MS-191

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BUSPIRONE HCL/MS-186 REFRIGERATOR
BUTABARBITAL/MS-178
BUTACAINE/MS-99
BUTALBITAL/MS-260
BUTETHAL/MS-49
CAFFEINE/MS-53
CANNABINOL/MS-120 Refrigerator
CAPTOPRIL/MS-193
CARBAMZEPINE(REFRIGERATOR)/MS-161
CARBROMAL/MS-44
CARFENTANIL/MS-107
CARISOPRODOL/REFRIGERATOR/MS-156
CAULOPHYLLINE/MS 275 BATCH #1
CELCOXIB/MS-243 LOT C401493 CONTROL
CHLORDIAZEPOXIDE HCL/MS-77
CHLOROTESTOSTERONE ACETATE-4/MS-76
CHLOROTHIAZIDE/MS-26
CHLORPHENIRAMINE MALEATE/MS-25 Not controlled any longer
CHLORPROMAZINE HCL/MS-24
CITALOPRAM/MS-28 REFRIGERATOR
CLENBUTEROL/MS-228 REFRIGERATOR
CLINDAMYCIN/MS-190 REFRIGERATOR
CLOMIPHENE/MS-195 REFRIGERATOR
CLOMIPRAMINE HCL/MS-50
CLONAZEPAM/MS-56
CLONIDINE HCL/MS-23
CLOPIDOGREL BISULFATE(PLAVIX)/MS-258
CLORAZEPATE DIPOTASSIUM/MS-249
CLOZAPINE/MS-194
COCAINE/MS-278
CODEINE/MS-95
CYCLOBENZAPRINE HCL/MS-221
CYPROHEPTADINE HCL/MS-219
DEHYDROTESTOSTERONE-1/MS-129
DEMOXEPAM/MS-22
DESIPRAMINE HCL/MS-21
DESMETHYLDIAZEPAM/MS-263
DEXTROAMPHETAMINE/MS-140
DIAZEPAM/MS-57
DICLOFENAC SODIUM SALT/MS-224
DIETHYLENE GLYCOL/MS-123
DIETHYLPROPION HCL/MS-72
DIHYDROCODEINE BITARTRATE/MS-143
DILTIAZEM HCL/MS-285
DIMETHYL AMPHETAMINE HCL/MS-114
DIMETHYLTRYPTAMINE/MS-257
DIPHENHYDRAMINE HCL/MS-42

DIPHENOXYLATE HCL/MS-108
DIPHENYLHYDANTOIN(5,5)/MS-13
DIPHENYLPYRALINE/MS-62
DL-AMINOGLUTETHIMIDE/MS-238 SIGMA A-9657 LOT 043K0939
DOXEPIN HCL/MS-18
DROSTANOLONE/MS-75
ENALAPRIL/MS-152
EPHEDRINE (L)/MS-73
EPITESTOSTERONE/MS-74
ESTAZOLAM/MS-150
ESTRONE/MS-286
ETHYL AMPHETAMINE-N-DL/MS-113
ETHYLMORPHINE/MS-80
FAMCICLOVIR/MS-280
FENCAMFAMINE HCL/MS-40
FENFLURAMINE HCL/MS-39
FENOFIBRATE/MS-215
FENTANYL/MS-252
FINASTERIDE/MS-242 LOT R3180 CONTROL
FLUNITRAZEPAM/MS-61
FLUOROFENTANYL-P/MS-106
FLUOXETINE/MS-217
FLUOXYMESTERONE/MS-169
FLURAZEPAM HCL/MS-38
FUROSEMIDE/MS-288
GABAPENTIN/MS-157
GEMFIBROZIL/MS-225
GLUTETHIMIDE/MS-112
HALAZEPAM/MS-37
HALOPERIDOL/MS-163
HALPERIDOL/MS-36
HEROIN/MS-126
HYDROCODONE/MS-131
HYDROCORTISONE/MS-159
HYDROMORPHONE HCL/ MS-9
HYDROXYZINE/MS-160
IBUPROFEN/MS-35
IMIPRAMINE HCL/MS-34
ISOAMYL NITRITE/MS-273
ISOBUTYL NITRITE/MS-270
ISONIAZID/MS-239 SIGMA I3377 LOT 034K0623
ISOPROPYL NITRITE/MS-271
KETAMINE HCL/MS-41
KETOTIFEN/MS-208
LAMOTRIGINE/MS-283
LAMPA-LYSERGIC ACID N-(METHYLPROPYL)AMIDE/MS-33
LEVORPHANOL TARTRATE/MS-144

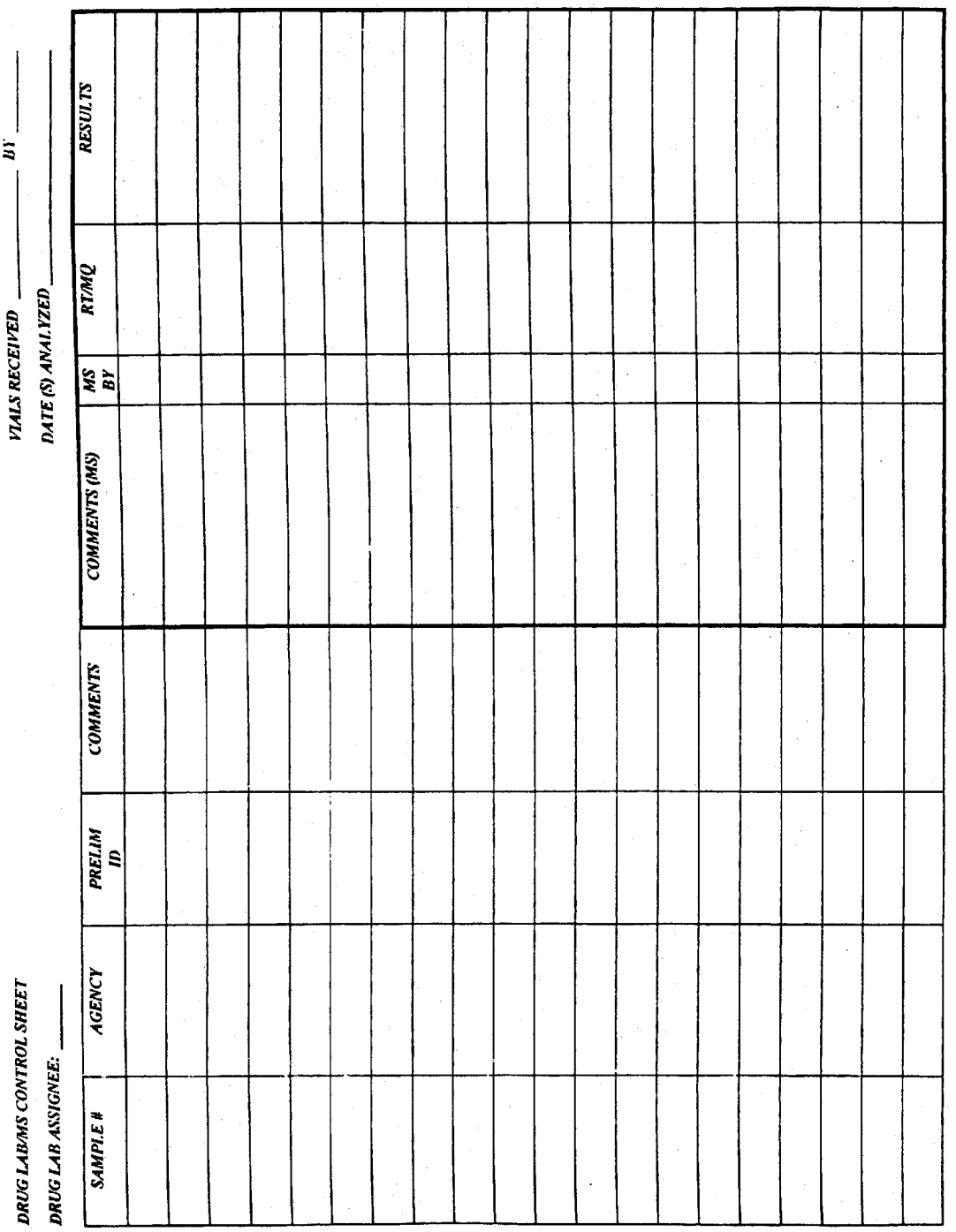
LIDOCAINE/MS-52
LOFENTANIL/MS-105
LORATADINE(CLARITIN)/MS-180
LORAZEPAM/MS-59
LOVASTATIN/MS-267
LOXAPINE SUCCINATE/MS-47
LYSERGIC ACID DIETHYLAMIDE TARTRATE/MS-115
LYSERGIC ACID/MS-54
MAPROTILINE HCL/ MS-1
MDE HCL/MS-90
MDPA HCL/MS-83
MDPB HCL-(±)-1(3,4-METHYLENEDIOXYPHENYL)-2-BUTANAMINE HCL/MS-109
MDPB(±)N-METHYL-(±)N-METHTL-1-(3,4-METHYLENEDIOXYPHENYL)-2-BUTANAMINE HCL/MS-111
MEDAZEPAM/MS-67
MEGESTROL ACETATE/MS-182
MEPERIDINE/MS-132
MEPIVACAINE HCL/MS-222
MEPROBAMATE/MS-82
MESCALINE/MS-266
MESTEROLONE/ MS-2
METAXALONE/MS-226
METHADONE-(DL)/ MS-10
METHAMPHETAMINE HCL (D)/MS-138
METHAMPHETAMINE HCL (L)/MS-137
METHANDRIOL DIPROPIONATE/MS-236
METHANDROSTENOLONE/MS-170
METHAQUALONE HCL/ MS-8
METHENOLONE ENANTHATE/MS-171 FREEZER
METHENOLONE/MS-71
METHIMAZOLE/MS-158
METHOCARBAMOL/ MS-3
METHYLCYTISINE-N/MS-121
METHYLDIHYDROTESTOSTERONE/MS-181 REFRIGERATOR
METHYLFENTANYL -3(±)/MS-103
METHYLFENTANYL(ALPA)/MS-102
METHYLPHENIDATE/MS-78
METHYLTESTOSTERONE/MS-197
METOCLOPRAMIDE HCL/MS-204
METOPROLOL TARTRATE/MS-174
METRONIDAZOLE/MS-214
MIDAZOLAM/MS-279
MIRTAZAPINE/MS-203
MONOACETYLMORPHINE-6 HCL/MS-100
MORPHINE/MS-259
MUSHROOM MIX/MS-276
NABUMETONE/MS-175

NALBUPHINE/MS-207
NALOXONE/MS-216 REFRIGERATOR MAKE UP IN RESIDUE VIAL
NALTREXONE HCL/MS-187 REFRIGERATOR
NANDROLONE DECANOATE/MS-149 REFRIGERATOR
NANDROLONE PHENPROPIONATE/MS-233 REFRIGERATOR
NANDROLONE PROPIONATE/MS-235
NANDROLONE/MS-87
NAPROXEN/MS-86
N-BUTYL NITRITE/MS-272
NEFAZODONE(CONTROL)/MS-166
NEVIRAPINE/MS-244 LOT 457793A CONTROL
NICOTINE-(S)-(-)/MS-122
NIFEDIPINE/MS-284 FREEZER
NITRAZEPAM/MS-66
NITROGLYCERIN/MS-213
NORDIAZEPAM/MS-79
NORETHANDROLONE/MS-45
NORETHINDRONE ACETATE/MS-153
NORPSEUDOEPHEDRINE (D)/MS-68
NORPSEUDOEPHEDRINE HCL-(L)/MS-17
NORTRIPTYLINE HCL/MS-85
NOSCAPINE/MS-124
ONDANSETRON/MS-118
OPIUM/MS-265
ORPHENADRINE HCL/MS-89
OXANDROLONE/MS-65
OXAPROZIN/MS-206
OXAZEPAM/MS-60
OXCARBAZEPINE(TRILEPTAL) /MS-250 CONTROL
OXYCODONE HCL/MS-31
OXYMETHOLONE/MS-154 REFRIGERATOR
OXYMORPHONE/MS-119
PAROXETINE(CONTROL)/MS-167
PENTOBARBITAL/MS-264
PERPHENAZINE SIGMA P-6402 LOT 064H0447/MS-240 REFRIGERATOR
PHENACETIN/ MS-5
PHENAZOPYRIDINE HCL/MS-176
PHENCYCLIDINE/MS-130
PHENDIMETRAZINE/MS-151
PHENMETRAZINE/MS-93
PHENOBARBITAL/MS-97
PHENOTHIAZINE/MS-84
PHENTAZOCINE/MS-81
PHENTERMINE/MS-15
PHENYLBUTAZONE/MS-247
PHENYLPROPANOLAMINE HCL/MS-12
PHENYTOIN/MS-165/DEUTERATED-DO NOT USE-SEE MS-13

P-HYDROXYNOREPHEDRINE/MS-269
PILOCARPINE HCL/MS-96
PIPERIDINOCYCLOHEXANE/MS-135
PRAZEPAM/MS-64
PROCAINAMIDE HCL/MS-88
PROCAINE HCL/MS-51
PROCHLORPERAZINE/MS-227
PROGESTERONE/MS-211
PROMETHAZINE HCL/MS-199
PROPANEDIOL-1,2/MS-125
PROPOXYPHENE/MS-155
PROPRANOLOL(REFRIGERATOR)/dl/MS-164
PSILOCYBIN/MS-127
PSILOCYN/MS-282 REFRIGERATOR
PYRILAMINE MALEATE/MS-177 NO LONGER CONTROLLED
QUETIAPINE FUMARATE/MS-234
SALICYLAMIDE/ MS-6
SALICYLIC ACID/ MS-7
SECOBARBITAL/MS-261
SERTRALINE HCL/MS-200
SILDENAFIL CITRATE/MS-237 VIAGRA EXPIRES 01-01-07 LOT 4002804 CONTROL
SODIUM BARBITAL/MS-262
SPIRONOLACTONE/MS-254
STANOZOLOL/MS-146 REFRIGERATOR
STRYCHNINE/MS-274
SULFAMETHOXAZOLE/MS-188
SUMATRIPTAN/MS-218
TAMOXIFEN(REFRIGERATOR)/MS-162
TEMAZEPAM/MS-63
TERBUTALINE/MS-229
TESTOSTERONE 17-PHENYLPROPIONATE/MS-110
TESTOSTERONE ACETATE/MS-184
TESTOSTERONE CYPIONATE/MS-145 REFRIGERATOR
TESTOSTERONE DECANOATE/MS-209
TESTOSTERONE ENANTHATE/MS-147 FREEZER
TESTOSTERONE PROPIONATE/MS-148
TESTOSTERONE/MS-192
TETRACAINE/MS-205
TETRAHYDROCANNABINOL-DELTA 9 OR DELTA 1/MS-117 Refrigerator
TETRAHYDROZOLINE/MS-185
THEOPHYLLINE MONOHYDRATE/MS-277
THIENYL FENTANYL/MS-101
THIETHYLPERAZINE MALEATE/MS-212
THIORIDAZINE HCL/MS-70
THIORIDAZINE/MS-134
TIZANIDINE HCL/MS-183
TOMOXETINE HBR/MS-256

TRAMADOL(CONTROL)/MS-168
TRAZODONE HCL/MS-14
TRENBOLONE ACETATE/MS-173 REFRIGERATOR
TRIAZOLAM/MS-19
TRIMETHOBENZAMIDE HCL/MS-202
TRIMETHOPRIM/MS-189 REFRIGERATOR
VALPROIC ACID/MS-251
VENLAFAXINE HCL/CONTROL TABLETS/MS-141
VERAPAMIL HCL/MS-16
WARFARIN/MS-248
YOHIMBINE HCL/MS-220
ZOLPIDEM(AMBIEN)/MS-253

Attachment 5



DRUG LAB/MS CONTROL SHEET

DRUG LAB ASSIGNEE: _____

VIALS RECEIVED _____ BY _____

DATE (S) ANALYZED _____

SAMPLE #	AGENCY	PRELIM ID	COMMENTS	COMMENTS (MS)	MS BY	RT/MQ	RESULTS

Folk_OIG_PRR_006439

Attachment 6

Drug Laboratory GC/MS Daily QC Check
MM/YY:_____

	System 4		System 5		System 6		System 7	
Day	Autotune	Inj/Column	Autotune	Inj/Column	Autotune	Inj/Column	Autotune	Inj/Column
1								
2								
3								
4								
5								
6								
7								
8								
9								
10								
11								
12								
13								
14								
15								
16								
17								
18								
19								
20								
21								
22								
23								
24								
25								
26								
27								
28								
29								
30								
31								

Comments:

QC Reviewer:_____ **QA Rewiewer:**_____
Date:_____ **Date:**_____

GC-MS QC.xls

Attachment 7

Common contaminants

Ions (*m/z*)	Compound	Possible source
18, 28, 32, 44 or 14, 16	H_2O, N_2, O_2, CO_2 or N, O	Residual air and water, air leaks, outgassing from Vespel ferrules
31, 51, 69, 100, 119, 131, 169, 181, 214, 219, 264, 376, 414, 426, 464, 502, 576, 614	PFTBA and related ions	PFTBA (tuning compound)
31	Methanol	Cleaning solvent
43, 58	Acetone	Cleaning solvent
78	Benzene	Cleaning solvent
91, 92	Toluene or xylene	Cleaning solvent
105, 106	Xylene	Cleaning solvent
151, 153	Trichloroethane	Cleaning solvent
69	Foreline pump oil or PFTBA	Foreline pump oil vapor or calibration valve leak
73, 147, 207, 221, 281, 295, 355, 429	Dimethylpolysiloxane	Septum bleed or methyl silicone column bleed
77, 94, 115, 141, 168, 170, 262, 354, 446	Diffusion pump fluid and related ions	Diffusion pump fluid
149	Plasticizer (phthalates)	Vacuum seals (O-rings) damaged by high temperatures, vinyl gloves
Peaks spaced 14 amu apart	Hydrocarbons	Fingerprints, foreline pump oil

Attachment 8-Standard Preparation QC Procedures

Every standard/control used by the GC/MS laboratory will have a QC folder. GC/MS Standard QC Form 1 will be prepared for all new standards or for new lots of a standard. Preparation of subsequent standards of the same lot will be recorded on GC/MS Standard QC Form 2. Every standard/control prepared by QC will document the preparing chemist, the manufacturer, the product number, the lot #, the assigned MS #, the expiration date, the preparation method, the sequence name, the acquisition method, and pertinent comments for non-routine standards. When a new QC folder is created, a reference copy of the Merck and Clarke's should be made for that compound. Solubility and boiling point can be found in the Merck and relevant mass spectral information from Clarke's can be compared to the instrument's library entries. A QC chemist/MS Supervisor will determine how to prepare the standard and which method it will be acquired on. If no method is suitable, the Mass Spectrometry Supervisor will create a new method if the standard is amenable to GC/MS analysis. A QC chemist will sign off on Form 1 or Form 2 if the standard is acceptable; it must have a clear, un-split apex and a mass spectrum that can be matched to reference spectrum. The standard will be placed into circulation on the date the QC chemist signs off on Form 1 or Form2. The MS Supervisor will review and sign off on the list of prepared standards at the end of the month for QA monitoring.

Drug Analysis Laboratory
GC/MS Standard QC
Form 1

Standard/Control:_____

Preparing Analyst:_____

Manufacturer of
Standard/Control:_____

Product #:_____

Lot #:_____

MS #:_____

Expiration Date:_____

Preparation:

Date of Preparation:_____ Solvent Used:_____

Amount of Standard Used (mg):_____ Approximate Concentration (mg/mL):_____

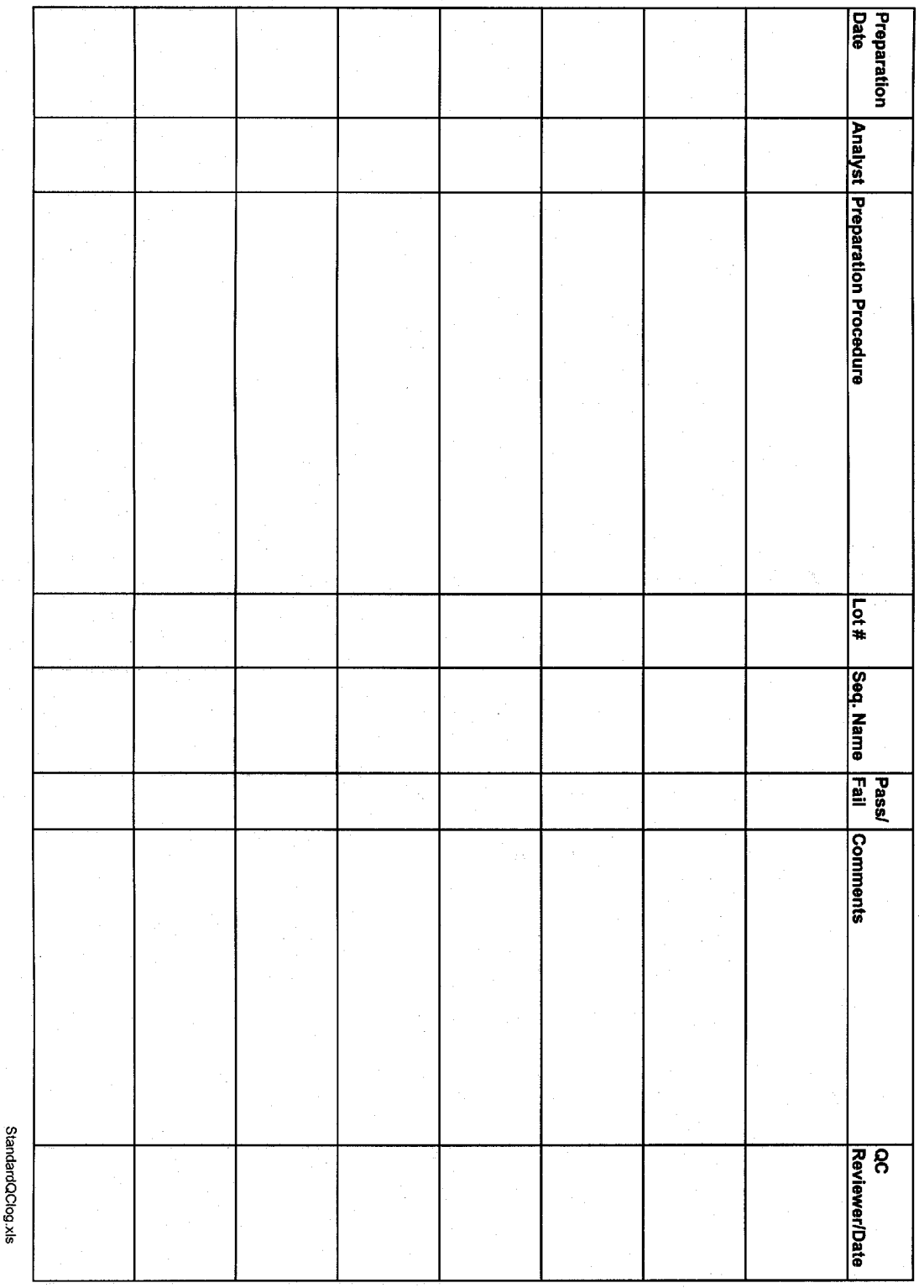
Volume of Solvent Used (mL):_____ QC sequence:_____

RESULTS: PASS/FAIL

COMMENTS:

Reviewer:_____
Signature Date

STANDARDQC.xls



Drug Analysis Laboratory
GC/MS Standard QC
Form 2

Preparation Date	Analyst	Preparation Procedure	Lot #	Seq. Name	Pass/ Fail	Comments	QC Reviewer/Date

StandardQClog.xls

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Drug Analysis Laboratory
Monthly GC/MS Standard QC

Preparation Date	Standard/Control	Pass/Fail	QC Reviewer/Date

QA Reviewer:_____ Date:_____

QAStandardlog.xls

Attachment 9

Analysis Date: System #4: Sequence File Name:

Analyst: System #5: Data File Names:

Setup Date: System #6:

Analyst: System #7:

1		26		51		76	
2		27		52		77	
3		28		53		78	
4		29		54		79	
5		30		55		80	
6		31		56		81	
7		32		57		82	
8		33		58		83	
9		34		59		84	
10		35		60		85	
11		36		61		86	
12		37		62		87	
13		38		63		88	
14		39		64		89	
15		40		65		90	
16		41		66		91	
17		42		67		92	
18		43		68		93	
19		44		69		94	
20		45		70		95	
21		46		71		96	
22		47		72		97	
23		48		73		98	
24		49		74		99	
25		50		75		100	

SequenceSheet.xls

Folk_OIG_PRR_006446

Attachment 10

GC/MS DAILY INJECTOR/COLUMN CHECK
COCAINE/CODEINE MIX
SYSTEM #:_____MM/YY:_____

COLUMN ID: _____ DATE INSTALLED:_____
TARGET ABUNDANCES: Cocaine: _____ Codeine: _____
INITIAL COCAINE RT: _____ INITIAL CODEINE RT: _____
INITIAL RELATIVE R.T. RATIO (Codeine/Cocaine): _____

DAY	INITIALS	SEQUENCE	ABUNDANCES		R.T.		RELATIVE R.T.	PERCENT DIFFERENCE	COMMENT
			Cocaine	Codeine	Cocaine	Codeine	Cod./Coc.		
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									
11									
12									
13									
14									
15									
16									
17									
18									
19									
20									
21									
22									
23									
24									
25									
26									
27									
28									
29									
30									
31									

QC COMMENTS:

QC REVIEWER:_____ DATE:_____

*If the relative R.T. isn't within +/-5% of the initial value and the abundance is less than 50% of the target values, notify supervisor.

COC-CODMIX.xls

Attachment 12

Vegas within a 24-hour period. The driver was arrested and charged with possession and delivery of a Schedule I controlled substance.

NDIC Comment: Stringent security measures at airports throughout the country have caused drug traffickers to use private and commercial vehicles to transport drugs via highways. In this case, the suspect flew to Seattle - a major Pacific Region drug distribution center - to obtain MDMA and rented a vehicle to drive the drug to Las Vegas - a major MDMA consumption market - avoiding detection by airport security.

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Selected Intelligence Brief

Anabolic Steroid Control Act of 2004 (Additional Information)

On October 22, 2004 the President signed into law the Anabolic Steroid Control Act of 2004, Public Law 108-358 (see *Microgram Bulletin* 2004;37(12):210). The new provision became effective January 20, 2005, and brought to 59 the total number of steroids controlled. Per numerous requests to the *Microgram* Editor, the 59 steroids are listed below:

(i) androstanediol:

(I) 3ß,17ß-dihydroxy-5α-androstane; and

(II) 3a,17ß-dihydroxy-5α-androstane;

(ii) androstanedione (5α-androstan-3,17-dione);

(iii) androstenediol:

(I) 1-androstenediol (3ß,17ß-dihydroxy-5α-androst-1-ene);

(II) 1-androstenediol (3a,17ß-dihydroxy-5α-androst-1-ene);

(III) 4-androstenediol (3ß,17ß-dihydroxy-androst-4-ene); and

(IV) 5-androstenediol (3ß,17ß-dihydroxy-androst-5-ene);

(iv) androstenedione:

(I) 1-androstenedione ([5α]-androst-1-en-3,17-dione);

(II) 4-androstenedione (androst-4-en-3,17-dione); and

(III) 5-androstenedione (androst-5-en-3,17-dione);

(v) bolasterone (7α,17α-dimethyl-17ß-hydroxyandrost-4-en-3-one);

(vi) boldenone (17ß-hydroxyandrost-1,4,-diene-3-one);

(vii) calusterone (7ß,17α-dimethyl-17ß-hydroxyandrost-4-en-3-one);

(viii) clostebol (4-chloro-17ß-hydroxyandrost-4-en-3-one);

(ix) dehydrochloromethyltestosterone (4-chloro-17ß-hydroxy-17α-methyl-androst-1,4-dien-3-one);

(x) Δ^1-dihydrotestosterone (a.k.a. "1-testosterone") (17ß-hydroxy-5α-androst-1-en-3-one);

(xi) 4-dihydrotestosterone (17ß-hydroxy-androstan-3-one);

(xii) drostanolone (17ß-hydroxy-2a-methyl-5α-androstan-3-one);

(xiii) ethylestrenol (17α-ethyl-17ß-hydroxyestr-4-ene);

(xiv) fluoxymesterone (9-fluoro-17α-methyl-11ß,17ß-dihydroxyandrost-4-en-3-one);

(xv) formebolone (2-formyl-17α-methyl-11a,17ß-dihydroxyandrost-1,4-dien-3-one);

(xvi) furazabol (17α-methyl-17ß-hydroxyandrostano[2,3-c]-furazan);

(xvii) 13ß-ethyl-17α-hydroxygon-4-en-3-one;

(xviii) 4-hydroxytestosterone (4,17ß-dihydroxy-androst-4-en-3-one);

(xix) 4-hydroxy-19-nortestosterone (4,17ß-dihydroxy-estr-4-en-3-one);

(xx) mestanolone (17α-methyl-17ß-hydroxy-5α-androstan-3-one);

(xxi) mesterolone (1a-methyl-17ß-hydroxy-[5α]-androstan-3-one);

(xxii) methandienone (17α-methyl-17ß-hydroxyandrost-1,4-dien-3-one);

(xxiii) methandriol (17α-methyl-3ß,17ß-dihydroxyandrost-5-ene);

(xxiv) methenolone (1-methyl-17ß-hydroxy-5α-androst-1-en-3-one);

(xxv) 17α-methyl-3ß, 17ß-dihydroxy-5α-androstane;

(xxvi) 17α-methyl-3a,17ß-dihydroxy-5α-androstane;

(xxvii) 17α-methyl-3ß,17ß-dihydroxyandrost-4-ene.

(xxviii) 17α-methyl-4-hydroxynandrolone (17α-methyl-4-hydroxy-17ß-hydroxyestr-4-en-3-one);

(xxix) methyldienolone (17α-methyl-17ß-hydroxyestra-4,9(10)-dien-3-one);

(xxx) methyltrienolone (17α-methyl-17ß-hydroxyestra-4,9-11-trien-3-one);

(xxxi) methyltestosterone (17α-methyl-17ß-hydroxyandrost-4-en-3-one);

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(xxxii) mibolerone (7α,17α-dimethyl-17ß-hydroxyestr-4-en-3-one);

(xxxiii) 17α-methyl-?1-dihydrotestosterone (17bß-hydroxy-17α-methyl-5α-androst-1-en-3-one) (a.k.a. "17-a-methyl-1-testosterone");

(xxxiv) nandrolone (17ß-hydroxyestr-4-en-3-one);

(xxxv) norandrostenediol:

(I) 19-nor-4-androstenediol (3ß,17ß-dihydroxyestr-4-ene);

(II) 19-nor-4-androstenediol (3a,17ß-dihydroxyestr-4-ene);

(III) 19-nor-5-androstenediol (3ß,17ß-dihydroxyestr-5-ene); and

(IV) 19-nor-5-androstenediol (3a,17ß-dihydroxyestr-5-ene);

(xxxvi) norandrostenedione:

(I) 19-nor-4-androstenedione (estr-4-en-3,17-dione); and

(II) 19-nor-5-androstenedione (estr-5-en-3,17-dione;

(xxxvii) norbolethone (13ß,17α-diethyl-17ß-hydroxygon-4-en-3-one);

(xxxviii) norclostebol (4-chloro-17ß-hydroxyestr-4-en-3-one);

(xxxix) norethandrolone (17α-ethyl-17ß-hydroxyestr-4-en-3-one);

(xl) normethandrolone (17α-methyl-17ß-hydroxyestr-4-en-3-one);

(xli) oxandrolone (17α-methyl-17ß-hydroxy-2-oxa-[5α]-androstan-3-one);

(xlii) oxymesterone (17α-methyl-4,17ß-dihydroxyandrost-4-en-3-one);

(xliii) oxymetholone (17α-methyl-2-hydroxymethylene-17ß-hydroxy-[5α]-androstan-3-one);

(xliv) stanozolol (17α-methyl-17ß-hydroxy-[5α]-androst-2-eno[3,2-c]-pyrazole);

(xlv) stenbolone (17ß-hydroxy-2-methyl-[5α]-androst-1-en-3-one);

(xlvi) testolactone (13-hydroxy-3-oxo-13,17-secoandrosta-1,4-dien-17-oic acid lactone);

(xlvii) testosterone (17ß-hydroxyandrost-4-en-3-one);

(xlviii) tetrahydrogestrinone (13ß,17α-diethyl-17ß-hydroxygon-4,9,11-trien-3-one);

(xlix) trenbolone (17ß-hydroxyestr-4,9,11-trien-3-one);

and any salt, ester, or ether of a drug or substance described in this list.

Attachment 13

Drug Scheduling

This document is a general reference and not a comprehensive list. This list describes the basic or parent chemical and does not describe the salts, isomers and salts of isomers, esters, ethers and derivatives which may also be controlled substances.

Schedule I			
Substance	**DEA Number**	**Non Narcotic**	**Other Names**
1-(1-Phenylcyclohexyl)pyrrolidine	7458	N	PCPy, PHP, rolicyclidine
1-(2-Phenylethyl)-4-phenyl-4-acetoxypiperidine	9663		PEPAP, synthetic heroin
1-[1-(2-Thienyl)cyclohexyl]piperidine	7470	N	TCP, tenocyclidine
1-[1-(2-Thienyl)cyclohexyl]pyrrolidine	7473	N	TCPy
1-Methyl-4-phenyl-4-propionoxypiperidine	9661		MPPP, synthetic heroin
2,5-Dimethoxy-4-ethylamphetamine	7399	N	DOET
2,5-Dimethoxyamphetamine	7396	N	DMA, 2,5-DMA
3,4,5-Trimethoxyamphetamine	7390	N	TMA
3,4-Methylenedioxyamphetamine	7400	N	MDA, Love Drug
3,4-Methylenedioxymethamphetamine	7405	N	MDMA, Ecstasy, XTC
3,4-Methylenedioxy-N-ethylamphetamine	7404	N	N-ethyl MDA, MDE, MDEA
3-Methylfentanyl	9813		China White, fentanyl
3-Methylthiofentanyl	9833		Chine White, fentanyl
4-Bromo-2,5-dimethoxyamphetamine	7391	N	DOB, 4-bromo-DMA
4-Bromo-2,5-dimethoxyphenethylamine	7392	N	Nexus, 2-CB, has been sold as Ecstasy, i.e. MDMA
4-Methoxyamphetamine	7411	N	PMA
4-Methyl-2,5-dimethoxyamphetamine	7395	N	DOM, STP
4-Methylaminorex (cis isomer)	1590	N	U4Euh, McN-422
5-Methoxy-3,4-	7401	N	MMDA

methylenedioxyamphetamine			
Acetorphine	9319		
Acetyl-alpha-methylfentanyl	9815		
Acetyldihydrocodeine	9051		Acetylcodone
Acetylmethadol	9601		Methadyl acetate
Allylprodine	9602		
Alphacetylmethadol except levo-alphacetylmethadol	9603		
Alpha-Ethyltryptamine	7249	N	ET, Trip
Alphameprodine	9604		
Alphamethadol	9605		
Alpha-Methylfentanyl	9814		China White, fentanyl
Alpha-Methylthiofentanyl	9832		China White, fentanyl
Aminorex	1585	N	has been sold as methamphetamine
Benzethidine	9606		
Benzylmorphine	9052		
Betacetylmethadol	9607		
Beta-Hydroxy-3-methylfentanyl	9831		China White, fentanyl
Beta-Hydroxyfentanyl	9830		China White, fentanyl
Betameprodine	9608		
Betamethadol	9609		
Betaprodine	9611		
Bufotenine	7433	N	Mappine, N,N-dimethylserotonin
Cathinone	1235	N	Constituent of "Khat" plant
Clonitazene	9612		
Codeine methylbromide	9070		
Codeine-N-oxide	9053		
Cyprenorphine	9054		
Desomorphine	9055		
Dextromoramide	9613		Palfium, Jetrium, Narcolo
Diampromide	9615		
Diethylthiambutene	9616		
Diethyltryptamine	7434	N	DET
Difenoxin	9168		Lyspafen
Dihydromorphine	9145		
Dimenoxadol	9617		
Dimepheptanol	9618		

Dimethylthiambutene	9619		
Dimethyltryptamine	7435	N	DMT
Dioxaphetyl butyrate	9621		
Dipipanone	9622		Dipipan, phenylpiperone HCl, Diconal, Wellconal
Drotebanol	9335		Metebanyl, oxymethebanol
Ethylmethylthiambutene	9623		
Etonitazene	9624		
Etorphine (except HCl)	9056		
Etoxeridine	9625		
Fenethylline	1503	N	Captagon,amfetyline,ethyltheophylline amphetamine
Furethidine	9626		
Gama Hydroxybutyric Acid (GHB)	2010	N	GHB, gama hydroxybutyrate, sodium oxybate
Heroin	9200		Diacetylmorphine, diamorphine
Hydromorphinol	9301		
Hydroxypethidine	9627		
Ibogaine	7260	N	Constituent of "Tabernanthe iboga" plant
Ketobemidone	9628		Cliradon
Levomoramide	9629		
Levophenacylmorphan	9631		
Lysergic acid diethylamide	7315	N	LSD, lysergide
Marijuana	7360	N	Cannabis, marijuana
Mecloqualone	2572	N	Nubarene
Mescaline	7381	N	Constituent of "Peyote" cacti
Methaqualone	2565	N	Quaalude, Parest, Somnafac, Opitimil, Mandrax
Methcathinone	1237	N	N-Methylcathinone, "cat"
Methyldesorphine	9302		
Methyldihydromorphine	9304		
Morpheridine	9632		
Morphine methylbromide	9305		
Morphine methylsulfonate	9306		
Morphine-N-oxide	9307		
Myrophine	9308		
N,N-Dimethylamphetamine	1480	N	

N-Ethyl-1-phenylcyclohexylamine	7455	N	PCE
N-Ethyl-3-piperidyl benzilate	7482	N	JB 323
N-Ethylamphetamine	1475	N	NEA
N-Hydroxy-3,4-methylenedioxyamphetamine	7402	N	N-hydroxy MDA
Nicocodeine	9309		
Nicomorphine	9312		Vilan
N-Methyl-3-piperidyl benzilate	7484	N	JB 336
Noracymethadol	9633		
Norlevorphanol	9634		
Normethadone	9635		Phenyldimazone
Normorphine	9313		
Norpipanone	9636		
Para-Fluorofentanyl	9812		China White, fentanyl
Parahexyl	7374	N	Synhexyl,
Peyote	7415	N	Cactus which contains mescaline
Phenadoxone	9637		
Phenampromide	9638		
Phenomorphan	9647		
Phenoperidine	9641		Operidine, Lealgin
Pholcodine	9314		Copholco, Adaphol, Codisol, Lantuss, Pholcolin
Piritramide	9642		Piridolan
Proheptazine	9643		
Properidine	9644		
Propiram	9649		Algeril
Psilocybin	7437	N	Constituent of "Magic mushrooms"
Psilocyn	7438	N	Psilocin, constituent of "Magic mushrooms"
Racemoramide	9645		
Tetrahydrocannabinols	7370	N	THC, Delta-8 THC, Delta-9 THC and others
Thebacon	9315		Acetylhydrocodone, Acedicon, Thebacetyl
Thiofentanyl	9835		Chine white, fentanyl
Tilidine	9750		Tilidate, Valoron, Kitadol, Lak, Tilsa
Trimeperidine	9646		Promedolum
Schedule II			

1-Phenylcyclohexylamine	7460	N	Precusor of PCP
1-Piperidinocyclohexanecarbonitrile	8603	N	PCC, precusor of PCP
Alfentanil	9737		Alfenta
Alphaprodine	9010		Nisentil
Amobarbital	2125	N	Amytal, Tuinal
Amphetamine	1100	N	Dexedrine, Biphetamine
Anileridine	9020		Leritine
Benzoylecgonine	9180		Cocaine metabolite
Bezitramide	9800		Burgodin
Carfentanil	9743		Wildnil
Coca Leaves	9040		
Cocaine	9041		Methyl benzoylecgonine, Crack
Codeine	9050		Morphine methyl ester, methyl morphine
Dextropropoxyphene, bulk (non-dosage forms)	9273		Propoxyphene
Dihydrocodeine	9120		Didrate, Parzone
Diphenoxylate	9170		
Diprenorphine	9058		M50-50
Ecgonine	9180		Cocaine precursor, in Coca leaves
Ethylmorphine	9190		Dionin
Etorphine HCl	9059		M 99
Fentanyl	9801		Innovar, Sublimaze, Duragesic
Glutethimide	2550	N	Doriden, Dorimide
Hydrocodone	9193		dihydrocodeinone
Hydromorphone	9150		Dilaudid, dihydromorphinone
Isomethadone	9226		Isoamidone
Levo-alphacetylmethadol	9648		LAAM, long acting methadone, levomethadyl acetate
Levomethorphan	9210		
Levorphanol	9220		Levo-Dromoran
Meperidine	9230		Demerol, Mepergan, pethidine
Meperidine intermediate-A	9232		Meperidine precursor
Meperidine intermediate-B	9233		Meperidine precursor
Meperidine intermediate-C	9234		Meperidine precursor
Metazocine	9240		
Methadone	9250		Dolophine, Methadose, Amidone

Methadone intermediate	9254		Methadone precursor
Methamphetamine	1105	N	Desoxyn, D-desoxyephedrine, ICE, Crank, Speed
Methylphenidate	1724	N	Ritalin
Metopon	9260		
Moramide-intermediate	9802		
Morphine	9300		MS Contin, Roxanol, Duramorph, RMS, MSIR
Nabilone	7379	N	Cesamet
Opium extracts	9610		
Opium fluid extract	9620		
Opium poppy	9650		Papaver somniferum
Opium tincture	9630		Laudanum
Opium, granulated	9640		Granulated opium
Opium, powdered	9639		Powdered Opium
Opium, raw	9600		Raw opium, gum opium
Oxycodone	9143		OxyContin, Percocet, Tylox, Roxicodone, Roxicet,
Oxymorphone	9652		Numorphan
Pentobarbital	2270	N	Nembutal
Phenazocine	9715		Narphen, Prinadol
Phencyclidine	7471	N	PCP, Sernylan
Phenmetrazine	1631	N	Preludin
Phenylacetone	8501	N	P2P, phenyl-2-propanone, benzyl methyl ketone
Piminodine	9730		
Poppy Straw	9650		Opium poppy capsules, poppy heads
Poppy Straw Concentrate	9670		Concentrate of Poppy Straw, CPS
Racemethorphan	9732		
Racemorphan	9733		Dromoran
Remifentanil	9739		Ultiva
Secobarbital	2315	N	Seconal, Tuinal
Sufentanil	9740		Sufenta
Thebaine	9333		Precursor of many narcotics
Schedule III			
Amobarbital & noncontrolled active ingred.	2126	N	Amobarbital/ephedrine capsules
Amobarbital suppository dosage	2126	N	

form			
Anabolic steroids	4000	N	"Body Building" drugs
Aprobarbital	2100	N	Alurate
Barbituric acid derivative	2100	N	Barbiturates not specifically listed
Benzphetamine	1228	N	Didrex, Inapetyl
Boldenone	4000	N	Equipoise, Parenabol, Vebonol, dehydrotestosterone
Buprenorphine	9064		Buprenex, Temgesic
Butabarbital	2100	N	Butisol, Butibel
Butalbital	2100	N	Fiorinal, Butalbital with aspirin
Chlorhexadol	2510	N	Mechloral, Mecoral, Medodorm, Chloralodol
Chlorotestosterone (same as clostebol)	4000	N	if 4-chlorotestosterone then clostebol
Chlorphentermine	1645	N	Pre-Sate, Lucofen, Apsedon, Desopimon
Clortermine	1647	N	Voranil
Clostebol	4000	N	Alfa-Trofodermin, Clostene, 4-chlorotestosterone
Codeine & isoquinoline alkaloid 90 mg/du	9803		Codeine with papaverine or noscapine
Codeine combination product 90 mg/du	9804		Empirin, Fiorinal, Tylenol, ASA or APAP w/codeine
Dehydrochlormethyltestosterone	4000	N	Oral-Turinabol
Dihydrocodeine combination product 90 mg/du	9807		Synalgos-DC, Compal
Dihydrotestosterone (same as stanolone)	4000	N	see stanolone
Dronabinol in sesame oil in soft gelatin capsule	7369	N	Marinol, synthetic THC in sesame oil/soft gelatin
Drostanolone	4000	N	Drolban, Masterid, Permastril
Ethylestrenol	4000	N	Maxibolin, Orabolin, Durabolin-O, Duraboral
Ethylmorphine combination product 15 mg/du	9808		
Fluoxymesterone	4000	N	Anadroid-F, Halotestin, Ora-Testryl
Formebolone (incorrect spelling in law)	4000	N	Esiclene, Hubernol
Hydrocodone & isoquinoline alkaloid 15 mg/du	9805		Dihydrocodeinone+papaverine or noscapine
Hydrocodone combination product	9806		Tussionex, Tussend, Lortab, Vicodin,

15 mg/du			Hycodan, Anexsia ++
Ketamine	7285	N	Ketaset, Ketalar, Special K, K
Lysergic acid	7300	N	LSD precursor
Lysergic acid amide	7310	N	LSD precursor
Mesterolone	4000	N	Proviron
Methandienone (see Methandrostenolone)	4000	N	
Methandranone	4000	N	?incorrect spelling of methandienone?
Methandriol	4000	N	Sinesex, Stenediol, Troformone
Methandrostenolone	4000	N	Dianabol, Metabolina, Nerobol, Perbolin
Methenolone	4000	N	Primobolan, Primobolan Depot, Primobolan S
Methyltestosterone	4000	N	Android, Oreton, Testred, Virilon
Methyprylon	2575	N	Noludar
Mibolerone	4000	N	Cheque
Morphine combination product/50 mg/100 ml or gm	9810		
Nalorphine	9400		Nalline
Nandrolone	4000	N	Deca-Durabolin, Durabolin, Durabolin-50
Norethandrolone	4000	N	Nilevar, Solevar
Opium combination product 25 mg/du	9809		Paregoric, other combination products
Oxandrolone	4000	N	Anavar, Lonavar, Provitar, Vasorome
Oxymesterone	4000	N	Anamidol, Balnimax, Oranabol, Oranabol 10
Oxymetholone	4000	N	Anadrol-50, Adroyd, Anapolon, Anasteron, Pardroyd
Pentobarbital & noncontrolled active ingred.	2271	N	FP-3
Pentobarbital suppository dosage form	2271	N	WANS
Phendimetrazine	1615	N	Plegine, Prelu-2, Bontril, Melfiat, Statobex
Secobarbital & noncontrolled active ingred	2316	N	various
Secobarbital suppository dosage form	2316	N	various
Stanolone	4000	N	Anabolex, Andractim, Pesomax, dihydrotestosterone

Stanozolol	4000	N	Winstrol, Winstrol-V
Stimulant compounds previously excepted	1405	N	Mediatric
Sulfondiethylmethane	2600	N	
Sulfonethylmethane	2605	N	
Sulfonmethane	2610	N	
Talbutal	2100	N	Lotusate
Testolactone	4000	N	Teslac
Testosterone	4000	N	Android-T, Androlan, Depotest, Delatestryl
Thiamylal	2100	N	Surital
Thiopental	2100	N	Pentothal
Tiletamine & Zolazepam Combination Product	7295	N	Telazol
Trenbolone	4000	N	Finaplix-S, Finajet, Parabolan
Vinbarbital	2100	N	Delvinal, vinbarbitone
Schedule IV			
Alprazolam	2882	N	Xanax
Barbital	2145	N	Veronal, Plexonal, barbitone
Bromazepam	2748	N	Lexotan, Lexatin, Lexotanil
Butorphanol	9720	N	Stadol, Stadol NS, Torbugesic, Torbutrol
Camazepam	2749	N	Albego, Limpidon, Paxor
Cathine	1230	N	Constituent of "Khat" plant
Chloral betaine	2460	N	Beta Chlor
Chloral hydrate	2465	N	Noctec
Chlordiazepoxide	2744	N	Librium, Libritabs, Limbitrol, SK-Lygen
Clobazam	2751	N	Urbadan, Urbanyl
Clonazepam	2737	N	Klonopin, Clonopin
Clorazepate	2768	N	Tranxene
Clotiazepam	2752	N	Trecalmo, Rize
Cloxazolam	2753	N	Enadel, Sepazon, Tolestan
Delorazepam	2754	N	
Dexfenfluramine	1670	N	Redux
Dextropropoxyphene dosage forms	9278		Darvon, propoxyphene, Darvocet, Dolene, Propacet
Diazepam	2765	N	Valium, Valrelease
Dichloralphenazone	2467	N	Midrin, dichloralantipyrine

Diethylpropion	1610	N	Tenuate, Tepanil
Difenoxin 1 mg/25 ug AtSO4/du	9167		Motofen
Estazolam	2756	N	ProSom, Domnamid, Eurodin, Nuctalon
Ethchlorvynol	2540	N	Placidyl
Ethinamate	2545	N	Valmid, Valamin
Ethyl loflazepate	2758	N	
Fencamfamin	1760	N	Reactivan
Fenfluramine	1670	N	Pondimin, Ponderal
Fenproporex	1575	N	Gacilin, Solvolip
Fludiazepam	2759	N	
Flunitrazepam	2763	N	Rohypnol, Narcozep, Darkene, Roipnol
Flurazepam	2767	N	Dalmane
Halazepam	2762	N	Paxipam
Haloxazolam	2771	N	
Ketazolam	2772	N	Anxon, Loftran, Solatran, Contamex
Loprazolam	2773	N	
Lorazepam	2885	N	Ativan
Lormetazepam	2774	N	Noctamid
Mazindol	1605	N	Sanorex, Mazanor
Mebutamate	2800	N	Capla
Medazepam	2836	N	Nobrium
Mefenorex	1580	N	Anorexic, Amexate, Doracil, Pondinil
Meprobamate	2820	N	Miltown, Equanil, Deprol, Equagesic, Meprospan
Methohexital	2264	N	Brevital
Methylphenobarbital (mephobarbital)	2250	N	Mebaral, mephobarbital
Midazolam	2884	N	Versed
Modafinil	1680	N	Provigil
Nimetazepam	2837	N	Erimin
Nitrazepam	2834	N	Mogadon
Nordiazepam	2838	N	Nordazepam, Demadar, Madar
Oxazepam	2835	N	Serax, Serenid-D
Oxazolam	2839	N	Serenal, Convertal
Paraldehyde	2585	N	Paral
Pemoline	1530	N	Cylert

Pentazocine	9709	N	Talwin, Talwin NX, Talacen, Talwin Compound
Petrichloral	2591	N	Pentaerythritol chloral, Periclor
Phenobarbital	2285	N	Luminal, Donnatal, Bellergal-S
Phentermine	1640	N	Ionamin, Fastin, Adipex-P, Obe-Nix, Zantryl
Pinazepam	2883	N	Domar
Pipradrol	1750	N	Detaril, Stimolag Fortis
Prazepam	2764	N	Centrax
Quazepam	2881	N	Doral, Dormalin
Sibutramine	1675	N	Meridia
SPA	1635	N	1-dimethylamino-1,2-diphenylethane, Lefetamine
Temazepam	2925	N	Restoril
Tetrazepam	2886	N	
Triazolam	2887	N	Halcion
Zaleplon	2781	N	Sonata
Zolpidem	2783	N	Ambien, Stilnoct,Ivadal
Schedule V			
Codeine preparations - 200 mg/100 ml or 100 gm			Cosanyl,Robitussin A-C,Cheracol,Cerose,Pediacof
Difenoxin preparations - 0.5 mg/25 ug AtSO4/du			Motofen
Dihydrocodeine preparations 10 mg/100 ml or 100 gm			Cophene-S, various others
Diphenoxylate preparations 2.5 mg/25 ug AtSO4			Lomotil, Logen
Ethylmorphine preparations 100 mg/100 ml or 100 gm			
Opium preparations - 100 mg/100 ml or gm			Parepectolin, Kapectolin PG, Kaolin Pectin P.G.
Pyrovalerone	1485	N	Centroton, Thymergix